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Pathology

EXPERIMENTAL PATHOLOGY

563. Electron Microscopy of Early Cytoplasmic Changes Due to Influenza Virus

C. G. HARFORD, A. HAMLIN, and E. PARKER. *Journal of Experimental Medicine* [*J. exp. Med.*] **101**, 577–590, June 1, 1955. 22 figs., bibliography.

Early changes in the bronchial epithelium of mice infected by the inhalation of aerosols containing the influenza virus were studied at Washington University School of Medicine, St. Louis, by electron microscopy of tissue sections. The results confirmed the authors' previous finding (*J. exp. Med.*, 1952, **95**, 173), in both ciliated and non-ciliated cells, of cytoplasmic inclusion bodies " composed largely of particles of a size estimated to correspond to the known size of influenza virus ". The same results were obtained with 3 strains of mouse-adapted Type-A virus and with 2 unadapted strains. Atypical cytoplasmic " linear formations ", seen most clearly in ciliated cells, were also present and were interpreted as abnormalities of the endoplasmic reticulum. No constant spatial relationship could be established between these " linear formations " and the inclusion bodies, nor could the authors' initial finding that changes in the endoplasmic reticulum preceded the appearance of inclusion bodies be conclusively confirmed. It was impossible to detect any difference between the microvilli found on the ciliated border of the epithelial cells of infected animals and those found in control animals; these observations therefore afford no support to the theory that the virus grows on cellular surfaces.

R. J. Ludford

564. Studies on Influenza Infection in Ferrets by Means of Fluorescein-labelled Antibody. I. The Pathogenesis and Diagnosis of the Disease. II. The Role of " Soluble Antigen " in Nuclear Fluorescence and Cross-reactions

CH'IEN LIU. *Journal of Experimental Medicine* [*J. exp. Med.*] **101**, 665–676 and 677–686, June 1, 1955. 15 figs., 32 refs.

The first part of this paper from Harvard Medical School reports observations on the sequence of pathological changes in the cells of the respiratory tract of ferrets following their intranasal inoculation with influenza virus of both Type A and Type B. By staining tissue sections with fluorescein-labelled antibody the presence of specific influenza viral antigens was demonstrated in both the cytoplasm and the nuclei of ciliated epithelial cells from the nasal turbinates of infected animals. Initially, the fluorescence was confined to a small part of the nasal epithelium and no appreciable abnormality was detectable in sections stained with haematoxylin and eosin, but it soon spread to involve the entire epithelium. This was followed by desquamation, coinciding with the onset of manifest illness. Pneumonia occurred in some of the infected ferrets, and viral antigens were found to have spread to the bronchial epithelium and mediastinal lymph nodes, a parallel rise occurring in the viral infectivity titre. Many desquamated ciliated epithelial cells and macrophages containing viral antigen were found in nasal smears, but usually only during the febrile period, and it is suggested that this observation might constitute the basis of a method for the rapid specific diagnosis of influenzal infection.

The investigation of cross-reaction between three strains of influenza A virus—PR8, Farrington, and Fm—on staining with fluorescein-labelled antibody is described in the second part. The nuclei of infected ciliated epithelial cells apparently contain a higher concentration of influenza viral antigens than does the cytoplasm, since the nuclear fluorescence was usually brighter than the cytoplasmic fluorescence, and the former was the chief manifestation of cross-reactions among the three strains. Cross-absorption experiments with preparations of the V and " soluble " (S) antigens of the virus strains showed that the S antigen was responsible for the nuclear fluorescence and for the cross-staining reactions.

R. J. Ludford

565. The Distribution of Poliomyelitis Virus in Cynomolgus Monkeys following Oral Administration, Tonsillectomy, and Intramuscular Injection of Diphtheria Toxoid. [In English]

J. D. VERLINDE, A. KRET, and R. WYLER. *Archiv für die gesamte Virusforschung* [*Arch. ges. Virusforsch.*] **6**, 175–182, 1955. 23 refs.

In a study carried out at the Netherlands Institute for Preventive Medicine, Leiden, the authors found that in cortisone-treated cynomolgus monkeys which had been infected with poliomyelitis virus by feeding them for 2 days with the Mahoney strain of Type-1 or the Saukett strain of Type-3 poliomyelitis virus and then bled to death after various intervals, the primary site of infection, multiplication, and excretion of the virus seemed to be the tonsils. From this site viraemia regularly developed and was demonstrable from the 5th to the 8th day after infection. During the period

of viraemia the virus could be demonstrated in the spleen, muscle tissue, lymph nodes, gastro-intestinal wall, nerve plexus, and peripheral ganglia. In animals infected with Type-3 virus it was also recovered from the wall of the colon before the development of viraemia, but the presence of virus in the gastro-intestinal wall and the faeces was only transitory, suggesting that the intestinal phase is not very important in cynomolgus monkeys. The virus could be demonstrated in the central nervous system only from the 3rd day after the last day of the viraemia, a finding which suggests that the central nervous system may not be invaded by direct haematogenous spread, but by secondary neural spread after haematogenous invasion of the peripheral nerves and ganglia.

In monkeys fed the Saukett strain of Type-3 poliomyelitis virus before and after tonsillectomy, the virus could be demonstrated in the glossopharyngeal nerve before and during the subsequent viraemia in tonsillectomized animals, but not in non-tonsillectomized animals. This suggests that the appearance of the bulbar form of poliomyelitis after tonsillectomy may be the result of primary neural spread.

These monkeys were also given an intramuscular injection into the right thigh of diphtheria toxoid precipitated by aluminium phosphate. Poliomyelitis virus could be demonstrated in the corresponding sciatic nerve from the 3rd day of viraemia, indicating the probability of secondary neural spread after haematogenous invasion of muscle damaged by the injection. *A. Ackroyd*

566. **Significance of the Level of Serum Aldolase in Tumor-bearing Animals**
J. A. SIBLEY, G. A. FLEISHER, and G. M. HIGGINS. *Cancer Research* [*Cancer Res.*] **15**, 306–314, June, 1955. 9 figs., 9 refs.

The significance of the increased serum aldolase level in tumour-bearing mice is discussed in this paper from the Mayo Clinic. In rats with implanted Walker carcinosarcoma 256 the serum aldolase level is several times higher than normal when the tumours have grown large. It is suggested that the tumour itself is the source of the excess aldolase present in the serum, a suggestion which is supported by the following findings: (1) after excision of the tumour the serum aldolase level falls rapidly to normal; (2) a significantly higher aldolase content is found in the blood from a vein leaving the tumour than in heart blood obtained at the same time; (3) the experimental production in animals without tumour of marked anaemia or extreme cachexia, comparable to that seen in tumour-bearing rats, has no influence on the serum level of aldolase; (4) splenectomy or adrenalectomy has no effect on the serum aldolase level and does not prevent the increase in that level in tumour-bearing rats, from which it would seem unlikely that the hyperplasia of the adrenal glands and spleen observed in tumour-bearing rats plays any part; (5) the aldolase content of the tissues of tumour-bearing rats was similar to that of normal animals, which does not suggest that tissue other than that of the tumour is the source of the excess aldolase. The serum level of aldolase was not raised until the tumour had become large, and it is suggested that the increased liberation of the enzyme derives from foci of necrosis in the tumour and is not characteristic of malignant tissue *per se*.
L. A. Elson

567. **Serum Aldolase in Experimental Liver Necrosis**
J. A. SIBLEY, G. M. HIGGINS, and G. A. FLEISHER *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **59**, 712–716, June, 1955. 6 figs., 7 refs.

The serum level of the glycolytic enzyme aldolase is consistently higher in rats bearing large tumours than in normal rats [see Abstract 566] because of an excessive liberation of the enzyme into the blood stream by the tumour mass, and it has been suggested that the source of the excess enzyme is the continuous breakdown of a large number of tumour cells which are rich in aldolase. It has already been found that the occurrence of abnormally high serum aldolase levels in human subjects can be correlated with the presence of acute, extensive injury to some tissue, as shown by the pronounced rise in patients with acute hepatitis in contrast to the practically normal level in patients with obstructive jaundice or cirrhosis.

At the Mayo Clinic an attempt was made to produce in the rat liver damage analogous to that seen in acute hepatitis in man, such destruction of a functional tissue resulting in a non-malignant condition, characterized by necrosis, which would further test the hypothesis that excessive cytolysis is the principal cause of a raised serum aldolase level. It was found that the production of focal hepatic necrosis in the rat by inhalation of carbon tetrachloride vapour resulted in a profound, but transient, increase in the serum aldolase level. The histological changes in the liver and the variations in the serum aldolase level under these conditions were considered comparable to the changes observed in acute hepatitis in man. Intravenous injection of a solution of crude papain produced similar liver changes and an increase in the serum aldolase level, but injection of a solution of crystalline papain of equal proteolytic activity had no such effect. There was no change in the serum aldolase level in experimental obstructive jaundice in the rat. *L. A. Elson*

568. **Experimental Arteriopathy. Spontaneous, Epinephrine–Thyroxine, and Cholesterol-induced Forms**
Y. T. OESTER, O. F. DAVIS, and B. FRIEDMAN. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 717–724, July–Aug., 1955. 18 refs.

The authors have studied, at the Stritch School of Medicine, Chicago, the effect of adrenaline and cholesterol in causing experimental arteriopathy in rabbits. It has been stated that atherosclerosis frequently occurs spontaneously in this species, but of a control group of 84 rabbits the authors found evidence of spontaneous arteriopathy of the aorta in only one.

A first group of 60 rabbits were treated daily for 15 days with slow intravenous injections of adrenaline, starting with a dose of 25 μg. per kg. body weight and increasing gradually to 50 μg. on the fifth day, this dose

being maintained for the remaining 10 days. At the same time an aqueous preparation of thyroxine was administered subcutaneously in a dose of 0·15 mg. per kg. body weight daily throughout the 15 days. Twelve of the animals died within 6 days; of the 48 survivors, 43 showed non-atheromatous lesions of the aortic media, often very severe and sometimes involving the intima as well.

The second experimental group of 43 rabbits were given intravenous injections of a cholesterol suspension, of which 40 mg. per kg. body weight (given in 2 doses of 20 mg. separated by at least 2 hours) was injected daily for a total of 20 days; the cholesterol (25 mg. per ml.) was suspended in distilled water with 9 mg. of sodium chloride, 9 mg. of benzyl alcohol, 5 mg. of sodium carboxymethylcellulose, and 4 mg. of "tween 80". In addition these animals received 300 mg. of cholesterol subcutaneously twice daily from the 10th to the 20th day. In a further 12 animals the suspending vehicle alone was injected. Of the animals treated with cholesterol, 11 died within the first 6 days. Of the 32 survivors, 23 showed atheromatous lesions of the aorta, which were, however, relatively less extensive than the lesions induced by adrenaline and thyroxine. None of the animals given injections of the vehicle alone showed evidence of sclerosis. Lastly, 11 rabbits were treated with combined injections of adrenaline, thyroxine, and cholesterol under the same conditions as those described for each separately. Of these animals, 5 died within the first 6 days; in each of the remaining 6 there was severe sclerosis combining both types of arteriopathy, the intimal proliferation being notably more extensive than when cholesterol alone was used.

Robert de Mowbray

CHEMICAL PATHOLOGY

569. **Cholesterol Content of Various Formations of the Cerebral Cortex in Man.** (Содержание холестерина в различных образованиях большого мозга человека)

L. A. Plotnikova. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **55**, 282–286, 1955. 2 figs., 3 refs.

In a post-mortem study undertaken mainly to determine the total and combined cholesterol content of various areas of the cerebral cortex, the opportunity was taken to measure also the moisture content. It was found that this did not differ to any appreciable degree in different parts of the cortex itself; it was, however, notably less in the optic thalamus and subcortical nuclei than in the "cortical analysers", and higher in the olfactory bulbs.

The free cholesterol value, which represents about 80% of the total cholesterol content of the brain substance, also differed little from one area of cortex to another, except in the optic thalamus where sometimes it attained double the value seen in other cerebral tissues. In contrast, the combined cholesterol content varied markedly in different areas, being highest in the optic thalamus and lowest in the olfactory bulb. For example, it ranged from 0·06 to 0·14 g. per 100 g. in the olfactory bulb, 0·13 to 0·27 g. per 100 g. in areas 21/38 of the "auditory analyser" (middle temporal lobe), from 0·2 to 0·52 g. per 100 g. in the post-central gyrus, and from 0·43 to 0·99 g. per 100 g. in the optic thalamus. The author suggests that this variation in the combined cholesterol content is probably related to the proportion of myelinated nerve fibres present in different areas of the cortex.

L. Firman-Edwards

570. **The Nature and Clinical Significance of Pigments in the Cerebrospinal Fluid**

L. J. Barrows, F. T. Hunter, and B. Q. Banker. *Brain* [*Brain*] **78**, 59–80, 1955. 5 figs., 18 refs.

After a rapid review of the significant literature the authors report, from the Massachusetts General Hospital (Harvard Medical School), Boston, the results of serial spectrophotometric assays of 149 samples of pigmented cerebrospinal fluid (C.S.F.) from 68 patients with various disorders including cerebral haemorrhage, spinal block, and liver disease with jaundice. By means of a 10-mm. absorption chamber in the Carey constant-recording spectrophotometer continuous density curves of the centrifuged spinal fluids were obtained which revealed spectra of: (1) oxyhaemoglobin, which appeared at the onset of intracranial haemorrhage, attained maximum concentration in the first few days, and then gradually diminished; (2) bilirubin, detectable in the 2 or 3 days following haemorrhage, its level rising as that of oxyhaemoglobin fell and persisting for 2 or 3 weeks; it was the predominant pigment in loculated C.S.F., cyst fluids, and subdural effusions, and was also present in the xanthochromic C.S.F. of 10 out of 12 jaundiced patients; (3) methaemoglobin was present in the C.S.F. from patients with subdural and intracerebral haematoma and craniopharyngioma, and also in the intraventricular fluid from a patient with an intracerebral haematoma.

The identification of oxyhaemoglobin was confirmed by the benzidine test, that of bilirubin by the Van den Bergh reaction, and of methaemoglobin by the red colour appearing after the addition of 0·1% potassium cyanide solution.

Non-pigmented spinal fluids, including centrifuged supernatant fluids from 7 patients with "traumatic taps", showed no absorption curve in the visible spectrum.

M. Sandler

571. **Colour Production and Stability in the Folin and Wu Method of Blood Glucose Estimation**

S. Dische. *Journal of Clinical Pathology* [*J. clin. Path.*] **8**, 253–261, Aug., 1955. 10 figs., 15 refs.

The author describes, from the Royal Air Force Institute of Pathology, Halton, Bucks, a new modification of the well-known method of Folin and Wu for the estimation of blood glucose content, which he has evolved in order to obviate the rapid fading of the blue colour which often gives rise to inaccuracies in the estimation of its intensity by modern photo-electric colorimetric methods. Some of the factors influencing the rate of fading were first investigated. Dilution with

distilled water after the reaction between the reduced copper and the phosphomolybdic reagent (P.M.R.) was one factor. Other experiments, in which various concentrations of phosphoric acid were used as diluent, showed that the fading was considerable with lower concentrations, while higher ones caused an immediate loss of colour with but little subsequent fading up to 22 hours. The use of a 1-in-3 dilution of P.M.R. as diluent caused only a minor degree of fading, equal to that occurring in the undiluted reaction mixture, whereas an increase in the intensity of the colour occurred with higher concentrations of P.M.R. A series of reactions with the reduced copper solution were then carried out with varying strengths of P.M.R., performing the dilution to the full volume at the same time. The intensity of the blue colour at 22 hours was found to be related to the final concentration of P.M.R.

The fading was thus shown to be dependent upon variations in concentration of P.M.R., while the elimination of fading was helped by raising the acidity of the P.M.R. by the addition of 2·5% phosphoric acid. It was also shown that the initial colour production varied inversely with the temperature of the reduced-copper–P.M.R. reaction. The intensity of the colour was augmented in a non-specific manner not related to the glucose–reduced-copper factor by the effect of exposure to direct sunlight. The purity of the sodium carbonate in the reagent solution was found not to influence fading significantly. The author's recommended modification in technique of the standard method of Folin and Wu is to add to the mixture of blood filtrate and alkaline copper reagent, after heating in a boiling water bath for exactly 6 minutes and cooling for 2 to 3 minutes, 10 ml. of a reagent consisting of 150 ml. of standard phosphomolybdic reagent, 25 ml. of phosphoric acid (specific gravity 1·75), and 325 ml. of distilled water. The blue colour is measured photoelectrometrically with a red filter. *Harry Coke*

572. The Utility of the Blood Pepsin Assay in Clinical Medicine

H. M. Spiro, A. E. Ryan, and C. M. Jones. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 261–266, Aug. 18, 1955. 5 figs., 9 refs.

Conventional methods of studying gastric secretion have several disadvantages, not the least of which are the unpleasantness to some patients of gastric intubation and the fact that this may result in either inhibition or stimulation of secretion and thus seriously affect the accuracy of the results.

In 1952 Mirsky *et al.* (*J. Lab. clin. Med.*, **40**, 17) described a method for determination of the blood pepsin level, and stated that this value is believed to be in good correlation with gastric pepsin secretion. In this paper from the Massachusetts General Hospital, Boston, the present authors report their experience of the clinical use of a slightly modified version of this method. The main modification consisted in carrying out acidification to *p*H 2·3 (instead of *p*H 1·5), and the units of proteolytic activity mentioned below are therefore not equivalent to those of Mirsky *et al.*

The mean value for 99 patients without known gastro-intestinal disorder was 336 units (range 100 to 700 units); when a further 46 patients with gastro-intestinal disease not involving the stomach were included the mean activity for the whole group was 353 units (range 100 to 800 units). The values for 80% of the "normal" patients lay between 150 and 450 units. For a group of 97 patients with duodenal ulcer the mean value was 580 units, but 16 of the patients had values below 450 units. In 12 out of 20 patients with gastric ulcer the blood peptic activity was above 450 units, and in 8 below that level, while in 23 patients with gastric carcinoma the activity was above 400 units in 11 cases, but below it in the remaining 12.

The method was also found to be of some value for differential diagnosis among patients admitted to hospital with massive gastro-intestinal haemorrhage, helping to distinguish bleeding due to duodenal ulcer from that due to hepatic cirrhosis. Of 22 cirrhotic patients, all but one had values below 400 units, whereas only 2 out of 18 with duodenal ulcer had values below this level. Blood peptic activity values for small numbers of patients with hiatus hernia, oesophageal stricture, and subtotal gastrectomy are also reported.

[Although the values for blood peptic activity in patients with duodenal ulcer were generally higher than those in the control subjects, the wide range of values encountered tends to make the result for any individual patient of very limited diagnostic significance.]

M. J. H. Smith

573. An *ortho*-Tolidine Method for the Detection of Occult Blood in Faeces

J. Kohn and T. O'Kelly. *Journal of Clinical Pathology* [*J. clin. Path.*] **8**, 249–251, Aug., 1955. 2 figs., 7 refs.

Pure benzidine for use in testing faeces for the presence of occult blood is now difficult to obtain since its production was discontinued some 3 years ago on account of its carcinogenic properties, and the benzidine preparations still available are unreliable for the performance of this test. The authors, working at St. Mary's Hospital, Roehampton, Surrey, therefore describe an alternative method utilizing *ortho*tolidine, which has the advantage that its sensitivity can readily be adjusted by varying either the concentration or the proportions of the reagents, and is therefore flexible enough to suit any specific requirements in sensitivity. The routine technique recommended by the authors was standardized so that it is slightly less sensitive than the benzidine test. A test-tube technique is the usual procedure, but the method has been satisfactorily adapted to a slide-test technique, with the proviso that the faecal smears be prepared on a silicone-coated, water-repellant surface and a less sensitive (less concentrated) reagent solution employed.

The technique consists in boiling a portion of faeces the size of a pea in 5 ml. of water to produce a homogeneous suspension. Four drops of "working reagent" and 1 drop of hydrogen peroxide (20 volume) are placed in a test tube, left to stand one minute as a blank control, and then 1 drop of the faecal suspension added. A

positive reaction is indicated by the appearance of a green or blue colour within a minute; this colour change develops more slowly and lasts much longer than with benzidine. The intake of iron salts or of chlorophyll does not produce false positive results. The working reagent consists of equal parts of a stock 4% solution of *ortho*tolidine in ethanol, glacial acetic acid, and distilled water, and is stable at 4° C. for at least a month. The stock solution is stable for " a very long time " and its effectiveness is unimpaired by a partial precipitation which may occur at 4° C. *Harry Coke*

574. **The Diagnosis of Uraemia and Azotaemia Post Mortem.** (Zur Diagnose der Urämie und Azotämie an der Leiche)
H. RIEMENSCHNEIDER. *Frankfurter Zeitschrift für Pathologie* [*Frankfurt. Z. Path.*] **66**, 191–200, 1955. 26 refs.

The post-mortem diagnosis of uraemia may present difficulties in the absence of severe renal damage, the tissue changes caused by extrarenal azotaemia being insufficiently specific when unsupported by other evidence. The author has therefore attempted to assess the value of a simple chemical method of demonstrating the presence of excess nitrogenous material in the tissues, and after first reviewing the relevant literature he here presents the results of his investigations at the Darmstadt City Hospital. The method used was that first described by Fossel (*Zbl. allg. Path. path. Anat.*, 1947, **83**, 363), in which a small piece of stomach is excised within 12 hours of death and placed in a glass dish. One drop of N/10 sodium hydroxide solution is then placed on the mucosal surface and the whole covered with a glass cover, on the under-surface of which is a hanging drop of Nessler's reagent. If nitrogenous material is present in excess the ammonia liberated from the tissues causes darkening of the reagent or formation of an ochre-yellow precipitate, the reaction being regarded as positive if this change takes place within 30 seconds. Comparative tests with mucosa from the pyloric antrum and from the fundus showed that the former more frequently gave a positive result.

The test was carried out on tissue from 349 unselected necropsies. In 57 of these cases a clinical diagnosis of uraemia had been made ante mortem, gross renal damage from chronic glomerulonephritis or pyelonephritis being present in the majority. The reaction to Fossel's test was positive in 50 (87·7%) of these 57, and in 49 (16·8%) of the remainder in which azotaemia had not been suspected. In none of these 49 cases was primary renal involvement found, but in over one-half the patient had suffered from carcinoma with extensive metastases in the liver or from hepatic failure due to other causes, while others had uncontrolled diabetes—all these being potential causes of extrarenal azotaemia.

The comparatively high proportion of negative reactions in the uraemic group and of positive reactions in the remainder was probably due to defects in the method itself. Nevertheless the author considers that this test is a useful adjunct to other means of diagnosis, especially in cases of extrarenal azotaemia, owing to its simplicity and speed. *P. I. Reed*

HAEMATOLOGY

575. **New Hemoglobin in Normal Adult Blood**
H. G. KUNKEL and G. WALLENIUS. *Science* [*Science*] **122**, 288, Aug. 12, 1955. 2 figs., 7 refs.

It was found by the authors that by zone electrophoresis of haemoglobin from the blood of healthy adults in a starch slab with a barbitone buffer at *p*H 8·6 a more slowly migrating coloured component could be separated from normal adult haemoglobin (haemoglobin A). When this material was isolated from the starch block and concentrated by ultrafiltration it was found to be essentially free from haemoglobin A, and to be itself a haemoglobin. When haemoglobin A free from this material was isolated from the starch block it did not again give rise to the new component " despite various harsh procedures ". The absorption curves of the two haemoglobins for visible light were identical and no significant differences were found in the ultraviolet spectrum. Both had the same sedimentation rate in the ultracentrifuge. The new component, which was present in a number of specimens of normal haemoglobin examined, resembled haemoglobin E in its electrophoretic migration rate both at alkaline and at acid *p*H.

Quantitative analyses of the haemoglobin in the blood of 26 individuals, including normal persons and patients with a variety of chronic diseases, to determine the proportion of the new component present indicated a mean value of 2·6% of the total haemoglobin content, with a range of 1·8 to 3·5%. Whereas it was found in all normal individuals and in patients with various types of anaemia, the blood of newborn infants with predominantly foetal haemoglobin contained little or none. An increased proportion was present in the blood in thalassaemia minor, but not in thalassaemia major when a considerable proportion of foetal haemoglobin was present.

The authors also report briefly that in addition to the component described above normal adult blood was found to contain small amounts of a haemoglobin which migrates faster than haemoglobin A on zone electrophoresis in barbitone buffer. This haemoglobin was isolated, concentrated, and proved on repeated separation always to show the same rapid mobility.
H. Lehmann

576. **Hematologic Observations of the Course of Erythroblastosis Fetalis**
J. F. DESFORGES and L. G. O'CONNELL. *Blood* [*Blood*] **10**, 802–811, Aug., 1955. 4 figs., 11 refs.

At Boston City Hospital the authors studied serial specimens of peripheral blood from 38 infants suffering from erythroblastosis foetalis. In 21 cases an exchange transfusion was necessary which was followed immediately by a reduction in the serum bilirubin level and also in the numbers of nucleated erythrocytes and reticulocytes, although both these types of cell reappeared transiently within 3 days. In most cases the platelet count fell immediately after transfusion to below 100,000 per c. mm., and rose gradually after 3 days. In infants

who did not receive a transfusion because they were only mildly affected the platelet count varied.

In both groups of infants the haemoglobin concentration declined in the first 3 months to an average of 7·6 g. per 100 ml., erythropoiesis then becoming adequate for return to normal levels. The degree of anaemia in this hypoplastic phase could not be correlated with the presence of antibody, with the blood group of the infant, or with any other factor. The majority of the erythrocytes were found to be more fragile than normal cells in hypotonic solutions, even when haemolysis was not excessive, and in some patients the erythrocytes showed increased mechanical fragility until the phase of anaemia began to regress. The responses to these two forms of physical stress could not be correlated with other manifestations of the disease, and the authors suggest that they may not be related to the haemolytic mechanism. *T. B. Begg*

577. **The Significance of a Positive L.E. Phenomenon**
R. S. Weiss and S. Swift. *Archives of Dermatology* [*Arch. Derm.* (*Chicago*)] **72**, 103–112, Aug., 1955. 24 figs., 33 refs.

The specificity of the L.E.-cell phenomenon was studied at Washington University, St. Louis, Missouri, two techniques being used which gave identical results—namely, the two-hour clot technique and that of Barnes and Moffatt in which suspect serum is added to a normal buffy coat. No L.E. cells were found in blood specimens from 24 patients suffering from penicillin reactions, but they were present in 3 out of 16 from patients receiving hydrallazine who had developed some symptoms attributed to the drug. In the course of the study cells were seen in which the ingested body had retained a sharp outline but in which there was no remaining chromatin pattern. These cells, which the authors term " advanced tart cells ", were observed in acute and subacute disseminated lupus erethymatosus, in rheumatoid arthritis, and in the hydrallazine syndrome. As true L.E. cells were sometimes seen in later preparations from the same patients these cells are regarded as precursors of some L.E. cells.

In preparations from 350 patients with a variety of other diseases no L.E. cells were found. *E. G. Rees*

578. **Demonstration of A and B Antigens in Human Leucocytes by Absorption and Elution Tests.** (Mise en évidence des antigènes A et B dans les leucocytes humains par des épreuves d'absorption et d'élution)
L. Berroche, B. Maupin, P. Hervier, and J. Dausset. *Vox sanguinis* [*Vox Sanguinis* (*Amst.*)] **5**, 82–93, Aug., 1955. 1 fig., 12 refs.

In this paper from the French Army and National Blood Transfusion Centres, Paris, the authors are not concerned with the alleged existence of specific antigens in leucocytes, but only with the group antigens corresponding with those of the erythrocytes, omitting entirely the question of Rh groups. Thus they confine themselves to the methods of demonstrating the factors A and B in human leucocytes, using the techniques of absorption and elution (the details of which are fully described in the original). They show that there is a marked difference in agglutinogen content between leucocytes from subjects in sub-groups A_1 and A_2. Platelets also appear to possess the same group characters as leucocytes. The eluates of leucocytes which have been used for absorption possess the agglutinins anti-A or anti-B.

The authors conclude that human leucocytes carry antigens A and B, corresponding to the erythrocytes of the same individual. Leucocytes did not react specifically with anti-O. They suggest the probability that the presence of antigens of the ABO system, acting on leucocytes, is of importance in transfusion.

A. Piney

579. **The Value of a Serum and Albumin Mixture for Use in the Detection of Blood Group Antigen–Antibody Reactions**
F. Stratton and E. R. Dimond. *Journal of Clinical Pathology* [*J. clin. Path.*] **8**, 218–224, Aug., 1955. 8 refs.

The investigations described in this paper from the Regional Blood Transfusion Service, Manchester, were designed to determine whether the test using 20% bovine albumin for the detection of incomplete antibodies—which is open to criticism on a number of grounds—could be improved by substituting a mixture of human serum and bovine albumin as the diluent. In a series of tests a comparison was made between the results with 20% bovine albumin and those with a mixture of equal parts of human serum and 30% bovine albumin; saline solution and often human serum alone were included in the comparisons. In all cases the human serum used as diluent was derived from blood of Group AB. [The original paper should be consulted for full details of the techniques employed.]

The authors comment that some of the defects of the albumin test can be remedied by using the serum–albumin mixture instead of the 20% albumin. In their experience the mixture has the following advantages: (1) it reduces the risk of zoning but does not abolish it; (2) it detects some low-grade D^u cells missed by the other method; (3) it detects some Rh antibodies not demonstrated by the antiglobulin (Coombs) technique; and (4) it detects anti-Kell antibodies. They therefore conclude that the use of the serum–albumin mixture is a considerable improvement on that of the 20% bovine albumin in cross matching, particularly if the test is made in the form of a titration. They recommend, however, that for cross-matching a saline agglutination method in tubes at room temperature and at 37° C. coupled with an antiglobulin technique is preferable.

A. S. Douglas

580. **The Normal Blood Clotting Time in the Light of Experience with the " Two-Syringe " Technique**
J. G. Alexander. *Journal of Clinical Pathology* [*J. clin. Path.*] **8**, 227–228, Aug., 1955. 7 refs.

The blood coagulation time was estimated by means of a two-syringe modification of the method of Lee and White in 30 healthy adults at De la Pole Hospital, Willerby, Yorkshire. Blood was collected into the first syringe with a minimum of venous trauma; the syringe

was then removed and a second one was fitted on to the needle, which was held as motionless as possible in the vein. The blood from each syringe was delivered into a standard tube and the coagulation time of each specimen determined. [The original paper should be consulted for the details of the procedure.] When the needle was held motionless during the change of syringe the coagulation time of the blood in the second syringe was longer than that of the blood in the first. When the needle was inadvertently moved during the change of syringe the coagulation time of the blood in the second tube was about the same as that in the first. The author concludes that even slight injury to the intima of a vein liberates sufficient thromboplastin to shorten the coagulation time significantly. *A. S. Douglas*

581. **Studies on the Antithrombin and Heparin Cofactor Activities of a Fraction Adsorbed from Plasma by Aluminum Hydroxide**

F. C. MONKHOUSE, E. S. FRANCE, and W. H. SEEGERS. *Circulation Research* [*Circulat. Res.*] **3**, 397–402, July, 1955. 3 figs., 14 refs.

The relationship between the heparin co-factor and the antithrombin activity of plasma has hitherto been obscure. However, in studies carried out at Wayne University College of Medicine, Detroit, the present authors have devised a quantitative chemical method for the determination of plasma antithrombin. The method, which is described clearly and in detail, involves the adsorption of the antithrombin on aluminium hydroxide and its subsequent elution. By fractionation with ammonium sulphate the concentration of antithrombin was increased eightfold. This concentrate, which was used in a series of observations, also manifested heparin co-factor activity to an equally augmented degree, and neutralization of antithrombin activity also neutralized the heparin co-factor activity.

The authors conclude that although the two activities correspond to the requirements for two distinct chemical reactions, they seem to involve the same molecule. They suggest the possibility that the two distinct phenomena are dependent upon the activity of one substance, or even upon the same molecular group.

H. Payling Wright

582. **An Evaluation of Paraffin Sections of Aspirated Bone Marrow in Malignant Lymphomas**

J. D. PETTET, G. L. PEASE, and T. COOPER. *Blood* [*Blood*] **10**, 820–830, Aug., 1955. 4 figs., 7 refs.

An attempt was made at the Mayo Clinic to assess the value of examination of smears and paraffin sections of aspirated bone marrow in the diagnosis of malignant lymphoma. In 9 out of 34 cases of Hodgkin's disease paraffin sections revealed focal or diffuse pleomorphic infiltrations which were diagnostic of the disease. Marrow smears showed Reed–Sternberg cells in 2 of these, but no helpful features in the other 7. In sections from 5 of the 34 cases small, non-specific granulomata were noted. The diagnosis was based on the bone-marrow appearances alone in only 3 cases. Diffuse or focal infiltrations of large, eosinophilic, reticular cells were seen in marrow sections from 6 out of 11 cases of reticulum-cell sarcoma. In one additional case sections showed granulomata. The findings on examination of smears of the bone marrow were abnormal in only 3 cases in this group.

Interpretation of the histological appearances proved most difficult in 21 cases of lymphocytic lymphosarcoma. Marrow sections were diagnostic in 6 instances and suggestive in 5 others; in all 11 instances marrow smears contained immature lymphocytes, which were diagnostic in 3 and suggestive in 8. In 6 cases the final diagnosis was based on the bone-marrow findings alone. Both sections and smears were unhelpful in 6 cases of follicular lymphoma. They were suggestive in 3 cases in which the findings on lymph-node biopsy were conclusive.

Aggregations of benign lymphocytes gave rise to difficulties in some sections. They were fewer and more circumscribed than lymphomatous deposits, occasionally had " reaction centres ", often surrounded a small vessel, and were composed of small benign lymphocytes. In general, patients with marrow lesions tended to have more advanced disease, with severe anaemia or leucopenia, and thrombocytopenia, than those without such lesions; this was especially true of patients with Hodgkin's disease and, to a lesser extent, of those with reticulum-cell sarcoma.

The authors emphasize that serial paraffin sections are more valuable than a single section, that it is worth examining all material obtained in a " dry tap ", and that in some cases repeated marrow examination is necessary. *T. B. Begg*

MORBID ANATOMY AND CYTOLOGY

583. **Sarcoma Arising in Glioblastoma of the Brain**

I. H. FEIGIN and S. W. GROSS. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 633–653, July–Aug., 1955. 6 figs., 33 refs.

The 3 cases of cerebral tumour described in this paper from the Mount Sinai Hospital, New York, are of special interest because the neoplasm in each case was composed of two dissimilar malignant tissues, one tissue component being identified histologically as that of a glioblastoma and the other having the characteristic appearances of a spindle-celled fibrosarcoma. The authors deprecate the designation of such tumours as " gliosarcoma ", a term originally used by Stroebe, who advocated that it should be restricted to tumours of glial origin within which a sarcoma derived from the walls of blood vessels could be distinguished. For many years the term gliosarcoma has been applied indiscriminately to any malignant gliomata in which there is a hyperplastic vascular reaction, but the authors consider that to use the term even in its original sense might lead to confusion of nomenclature. In one of the cases described the sarcomatous elements had grown more rapidly than the gliomatous tissue, the latter forming only a very small part of the whole tumour. It is suggested that some of the so-called primary sarcomata of the brain

may arise in a glioblastoma by sarcomatous changes in the blood vessels, with subsequent overgrowth of the sarcoma obscuring or destroying the glioblastoma; no trace of the original glioblastoma would then be found on histological examination. *Ruby O. Stern*

584. **A Clinical and Pathological Study of Cerebral Venous Trauma.** (Материалы к клинике и патологической анатомии венозных инсультов)
B. I. SHARAPOV. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **55**, 415–421, 1955. 4 figs., 18 refs.

Observations on 12 patients with traumatic or thrombotic cerebral lesions revealed the presence of venous aneurysms, with or without haemorrhages, in the ocular fundi. Similar pathological changes were demonstrated histologically post mortem in the small cerebral veins of the patients who died, accompanied by separation of the layers in the walls of the cerebral venules and small veins, extravasation of blood, and the formation of aneurysms.

Another post-mortem change observed was a triad of lesions in the ganglion cells (the " anterior nucleus " of the vagus) consisting in (1) swelling of the cytoplasm of the cell, (2) destruction of the rings and filaments of the " pericellular apparatus ", and (3) lamination of the walls of the capillary adjacent to the cell. The author suggests that the pericellular apparatus [which apparently consists of fine " rings and filaments " occurring on the walls of the nerve cell and of the accompanying capillary] may be an ending of the " multiple cerebral interreceptor ", the destruction of which would lead to trophic changes in the corresponding nerve cells and capillaries. *A. Swan*

585. **Absence of Chromosal Sex Differences in the Epidermal Structures of Basal Cell Carcinoma**
J. P. WEINMANN, J. MEYER, and A. S. MARWAH. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **25**, 43–54, July, 1955. 2 figs., 4 refs.

At the University of Illinois College of Dentistry, Chicago, sections of basal-cell tumours were examined for the presence or absence of the sex chromatin particle in the nuclei of cells in epithelial structures. An intranuclear chromatin particle, similar to that considered to be characteristic of the cells in females, was found in sections of basal-cell carcinomata from 11 male patients. The incidence of this particle was about half that observed in cells of a corresponding series of sections from female patients. The particle was not confined to malignant cells in male patients, but occurred also in the nuclei of epithelial cells in the epidermis, in hair follicles, and in sebaceous and sweat glands. Not all areas of sections of carcinomata showed this chromatin particle, and positive fields became less frequent as the distance from the tumour increased. However, the number of cells per field containing such a particle did not vary with the distance of the field from the tumour.

It is suggested that the appearance of a sex-chromatin-like particle in the nuclei of cells in epidermal structures in males is due to an alteration in the chromatin associated with the development of basal-cell carcinomata. Possibly all cells exhibiting this feature are potentially malignant, which implies that basal-cell carcinomata can originate from any of the epidermal structures.
R. J. Ludford

586. **Hemorrhage, Necrosis, and Cyst Formation in the Thyroid Gland**
N. JOHNSON. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **101**, 85–93, July, 1955. 10 figs., 20 refs.

Having observed that the literature contains little information on the causation of the degenerative changes often seen in thyroid nodules the author, at the University of Melbourne, studied the histological features of thyroid glands from 8 female patients, aged 25 to 60, in which there were nodules showing haemorrhage, necrosis, and cyst formation. In 4 cases the nodules, which were foetal adenomata, contained giant, thin-walled blood vessels. In only one case in the series was there evidence of arterial blockage. In 2 other cases there was degeneration in one part of a nodule and epithelial activity in another part.

From these findings and from his observations in a previous investigation (*Aust. N.Z. J. Surg.*, 1953, **23**, 95) the author considers that the degenerative changes resulting in ischaemia may be due either to occlusion of the nodular artery or one of its branches or to functional disturbances under nervous or humoral control, whereby shunts occur causing a redistribution of blood within the nodule. The result of these vascular changes depends on both the duration and the intensity of the disturbance, and may range from gradual atrophy of part of a nodule to frank necrosis of the whole structure. Secondary changes are haemorrhage, compatible with infarction seen elsewhere, and inflammation. In the author's view the massive thyroid haemorrhage which is occasionally seen may be due to other factors.
D. G. Adamson

587. **Interpretation of Tuberculous Lesions after Chemotherapy**
J. C. DICK. *Lancet* [*Lancet*] **2**, 216–223, July 30, 1955. 12 figs., bibliography.

In this paper from Stobhill Hospital, Glasgow, the significance of the changes in tuberculous lesions after chemotherapy is discussed. Tuberculous lesions are due to sensitization, there being no evidence of toxin formation; however, the striking difference between the changes in tuberculous lesions after streptomycin therapy and those observed after isoniazid therapy suggests that a toxin may be at work. After streptomycin " healing " is often associated with dense fibrosis, while after isoniazid scarring is much less and many early lesions resolve, suggesting that isoniazid liberates the tissues from some toxic influence. The feeling of general well-being experienced by patients given isoniazid supports this hypothesis. A combination of the two drugs is desirable not only because simultaneous resistance is unlikely, but also because streptomycin is more effective than isoniazid against secondary infection.

The persistence of organisms in many chronic lesions is due not to inaccessibility, but to the fact that these organisms are in a state of metabolic inactivity. Excision of these lesions is often justified because they may again become active. *D. M. Pryce*

588. **The Character of Tuberculous Cavities as Seen in Surgically Resected Specimens**
J. R. THOMPSON. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 158–170, 1955. 6 figs., 8 refs.

Variation in the type of lesion found in lungs resected for pulmonary tuberculosis is to be expected, since chemotherapy interrupts the disease process at different stages and different methods of healing may be associated with treatment with different agents. During a period of 3½ years 335 cases of pulmonary tuberculosis were treated by resection at the Chicago Municipal Tuberculosis Sanitarium and cavitation was present in 240 of the lungs or lobes removed. The most common type of cavity had a thick, fibrotic wall and there was marked bronchiectasis of the adjacent lung (66·3%). In 10·8% of cases there was a thin-walled tension cavity, in 10·4% there was extensive disease with irregular multiple cavities, and in 9·6% the cavity had a smooth, fibrous wall and there was practically no sign of activity in the surrounding lung (" open healing "). Cavities of this last type had no epithelial lining except near the mouths of communicating bronchi, and in 20 out of 23 cases the patient had received treatment with isoniazid. In 2·9% of cases the cavity was thought to result from liquefaction of a tuberculoma. *D. M. Pryce*

589. **Extrapulmonary Lesions in Interstitial Plasma-cell Pneumonia.** (Organveränderungen bei interstitieller, plasmacellulärer Pneumonie)
A. GOEBEL, W. OEHLERT, G. RUDOLPH, and P. SCHNEPPENHEIM. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] **76**, 340–350, 1955. 4 figs., bibliography.

Interstitial plasma-cell pneumonia, a serious and not uncommon disease among young infants on the Continent of Europe, was formerly regarded as a manifestation of congenital syphilis. Since its identification as a separate entity shortly before the second world war, and particularly since the discovery by Jirovec and Vanec in 1952 of *Pneumocystis carinii* in lungs of infants dying of the disease, many papers have been published describing the pulmonary lesions. This paper from the University of Cologne, on the other hand, deals with the anatomical changes found in organs other than the lungs in 34 fatal cases.

The heart muscle showed areas of rarefaction which were due to vacuolization or complete dissolution of muscle fibres. Empty sarcolemma-tubes (*Röhrenfasern*) were frequently seen. In the arteries all over the body oedematous swelling of the endothelium was found, the oedema often spreading through the whole vessel wall and into the periarterial tissue. The liver was congested and showed distension of the pericapillary lymph-spaces, with occasional giant cells. The kidneys in one-third of the cases showed nephrocalcinosis of the cortical area. The adrenal glands were enlarged and showed a decrease in their content of neutral fat, cholesterol, and ketosteroids. The changes are regarded by the authors as non-specific and due to the anoxaemia resulting from the pneumonia. *H. S. Baar*

590. **Post-traumatic Adrenal Apoplexy**
S. SEVITT. *Journal of Clinical Pathology* [*J. clin. Path.*] **8**, 185–194, Aug., 1955. 4 figs., 33 refs.

After a survey of the literature the author describes 14 cases of post-traumatic adrenal apoplexy occurring in a series of 50 necropsies performed at the Birmingham Accident Hospital. In 13 of these there were severe closed abdominal or thoracic injuries, but in the remaining case the lower limbs were chiefly involved and there was only slight abdominal trauma. The adrenal haemorrhage was bilateral in 3 cases and unilateral in 11. Fractured ribs with haemothorax or pneumothorax, rupture of the liver, spleen, or kidney, and fracture of pelvis were often present.

In every case the essential lesion in the adrenal gland was a firm, clotted haemorrhage of varying size, often surrounded by a stretched and occasionally ruptured cortex. Generally the haemorrhage was larger when the right side was involved. Histological examination showed a recent clot invading the cortex, and small patches of cortical necrosis probably due to local ischaemia caused by pressure. The bleeding was mostly from small fissures or tears in the walls of venules in the juxtamedullary cortex, which were considered to be due to direct violence in most cases. Incompatible blood transfusion was ruled out as a cause of bleeding in this series.

Although the associated injuries were sufficient to account for death in most of these cases, the adrenal haemorrhage might have been a contributory factor in some of them. Depletion of the adrenocortical lipid content was demonstrated in 8 out of 12 cases and splenic eosinopenia in 4, these being regarded as evidence of adrenal hyperactivity, but there were at least 2 cases in which no indication of activity was found either in the apoplectic or in the normal gland, suggesting " that adrenocortical failure due to inhibition of the glands had occurred ".

The mechanical aspects of adrenal haemorrhage and its dependence on the anatomical relations and histological structure of the gland are discussed. Apart from direct violence, the cause of the haemorrhage may be a sudden increase of pressure in the vena cava. The cortex may be directly destroyed or rendered ischaemic by the haemorrhage, or pressure from the central haemorrhage may possibly interfere with venous drainage so that the hormones secreted by the cortex never reach the blood stream.

(In an addendum it is reported that in a further series of 10 necropsies on patients with injuries comparable to those in the series reported above one case of incomplete right adrenal apoplexy, one of bilateral adrenal apoplexy, and one of bilateral complete haemorrhagic necrosis of the adrenal cortex and medulla were found.)
F. Hillman

591. **Fat Emboli in Glomerular Capillaries of Choline-deficient Rats and of Patients with Diabetic Glomerulosclerosis**

W. S. HARTROFT. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 381–397, May–June, 1955. 12 figs., 24 refs.

The author reports, from the University of Toronto, the results of a post-mortem search for fat emboli in the glomerular capillaries of over 150 rats which were fed on choline-deficient diets for periods of 4 to 18 months and in necropsy material from 16 diabetic patients with Kimmelstiel–Wilson lesions, 22 diabetics without evidence of such lesions, 20 patients with alcoholic cirrhosis, 7 with acute, subacute, or chronic glomerulonephritis, 2 with myxoedema, and one with xanthomatous biliary cirrhosis.

Most of the choline-deficient rats had developed hepatic cirrhosis, and fat emboli were present in the kidneys, lungs, and heart. Emboli were found in the arcuate and interlobular arteries and in other vessels, and most frequently in the capillaries of the glomerular tufts. In the region of the emboli the glomerular capillaries were distended with erythrocytes, indicating stasis, and the inflow of injected ink was arrested, suggesting that the changes were the result of obstruction of the blood flow by fat emboli. This was followed by focal degenerative changes in the walls of the glomerular capillaries, thickening of basement membranes, and the appearance of homogeneous eosinophilic material, suggesting the exudation of plasma in and between the capillary walls. Eventually considerable portions of the glomerular tuft were replaced by homogeneous material which stained with periodic-acid–Schiff and silver stains; stainable lipid was always found and cholesterol deposits could occasionally be demonstrated. These late changes closely resembled Kimmelstiel–Wilson lesions in man. The incidence of the lesions varied with the duration of choline deficiency and the sensitivity of the rats to it, as judged by the severity of the hepatic lesions. Extra-renal lesions such as myocardial fibrosis, aortic sclerosis, lipidosis of the coronary arteries, ceroid and fat deposits in the lymph nodes, and testicular atrophy were also found.

In regard to the human findings, fat was demonstrated within the glomerular capillaries and in other vessels in necropsy material from 12 of the 16 diabetics with Kimmelstiel–Wilson lesions, but to an even greater extent in the walls of the glomerular vessels, between the vessels and in Bowman's space, in the glomerular capsule, and even in the basement membranes of the tubules; some of the glomerular capillaries containing lipid were greatly dilated. However, in only 3 of the 22 diabetics without Kimmelstiel–Wilson lesions and in only 4 of the patients with alcoholic cirrhosis was fat found within the lumen of the glomerular capillaries. In none of the cases of glomerulonephritis, myxoedema, or biliary cirrhosis was fat found within the lumen, although it was often present in the vessel walls.

Summing up, the author considers fat embolism to be the primary lesion in the choline-deficient rats, since it was repeatedly observed in otherwise normal glomeruli and since glomerular lesions were rarely seen which did not contain fat. The similarity of the renal and extra-renal lesions in these rats and in patients with diabetes mellitus and the tendency of diabetic patients to develop hyperlipaemia together suggest that the plugging of glomerular capillaries with fat may be the starting point of Kimmelstiel–Wilson lesions in man.

Robert de Mowbray

592. **Fat Embolism in Diabetic Patients without Physical Trauma**

S. P. KENT. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 399–403, May–June, 1955. 15 refs.

The author has attempted to determine whether the fat emboli found in diabetic patients can be distinguished from those found in traumatic cases, notably traumatic fracture of bone. At the University of Alabama Medical Center, Birmingham, Alabama, he examined necropsy material from 53 diabetic patients and 53 non-diabetic subjects, none of whom had suffered recent trauma.

Fat emboli were found in 24 of the 53 diabetics (45·3%) and in only 11 of the non-diabetic cases (20·7%). The emboli could be differentiated from other sudanophilic material (present in the lungs in over 90% of cases) by their intravascular position and their tendency to conform to the lumen of the blood vessel. In most cases the emboli were few and small and probably of no clinical significance. In only 5 of the diabetics were fat emboli at all abundant. In all of these the disease had been poorly controlled, 4 having died in diabetic coma and one in hypoglycaemia. The fat emboli could not be differentiated from those found in traumatic cases.

Some degree of fatty change was found in the liver of all the diabetics; in 31 out of the 53 diabetic and in 18 out of the 53 non-diabetic patients fatty cysts were present. In all cases finely granular fatty material was found in the liver cells. The degree of fatty change was not necessarily correlated with the presence or degree of fat embolism.

Robert de Mowbray

593. **Male Tumours of the Ovary.** (Tumeurs mâles de l'ovaire)

P. LAFFARGUE. *Presse médicale* [*Presse méd.*] **63**, 959–961, June 22, 1955. 13 figs.

In this anatomical and pathological study from the Faculty of Medicine, Algiers, the author reviews the literature and classifies "male" tumours of the ovary into three types as follows. (1) Arrhenoblastoma resembling the embryonic male gonad in histological structure and containing columns of epithelial cells, which may undergo a tubular arrangement, together with interstitial cells of the Leydig type. These tumours are virilizing and about 20% of them are malignant. (2) Tubular arrhenomata or pure Sertoli-cell tumours. These give rise to little or no virilism and in fact do not appear to show much endocrine activity; they are invariably benign. (3) Pure endocrine tumours, usually designated as luteomata, adrenal rest tumours, or "masculinovoblastomata". These arise in the hilum of the ovary, are usually of small size, and give rise to severe degrees of virilism. In structure they resemble adrenocortical tissue or corpus luteum; they are occasionally malignant.

Robert de Mowbray

Microbiology and Parasitology

594. Tissue Culture Diagnosis of Poliomyelitis and Aseptic Meningitis

M. O. GODENNE and J. T. RIORDAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158,** 707–712, July 2, 1955. 3 figs., 12 refs.

The object of the investigation here reported from Yale University School of Medicine was to assess the value of tissue-culture methods in the laboratory diagnosis of poliomyelitis. Of the 96 cases of acute disease of the nervous system studied, the final diagnosis of paralytic poliomyelitis was made in 49, aseptic meningitis (or non-paralytic poliomyelitis) in 41, and encephalitis in 6. A series of 31 cases of miscellaneous febrile illness served as a control group. In each case monkey kidney tissue cultures were inoculated with material from throat and rectal swabs and stools, and in most cases with cerebrospinal fluid, all of which were obtained as soon after admission as possible. The cultures were examined for cytopathogenic effect every 2 to 4 days up to at least 12 days.

Poliomyelitis virus was isolated in 44 (90%) of the 49 cases of paralytic poliomyelitis, in 13 (32%) of the 41 cases of aseptic meningitis, and in 3 (50%) of the 6 cases of encephalitis, but in none of the cases in the control group. The virus was isolated from 46% of the throat swabs, 43% of the rectal swabs, and 89% of the stools tested in cases of paralytic poliomyelitis, the corresponding figures for cases of aseptic meningitis being 10, 17, and 34% and for cases of encephalitis 17, 17, and 33%. In contrast, the virus was isolated from only one out of 63 specimens of cerebrospinal fluid. Of the strains isolated, 83% were of Type 1 and 17% of Type 3. Isolation and typing were accomplished within one week of inoculation of cultures in 60% of the cases in which a positive culture was obtained and within 2 weeks in 88%. Examination of the patient's serum for neutralizing and complement-fixing antibodies at various stages of the disease revealed at least 7 different types of response and yielded diagnostically significant results in 96% of the virus-positive cases. Heterotypic as well as homotypic antibodies were demonstrated by both methods, but particularly by the complement-fixation test.

Joyce Wright

595. Comparison of Solid and Liquid Medium Sensitivity Tests of Tubercle Bacilli to *para*-Aminosalicylic Acid

D. A. MITCHISON and M. MONK. *Journal of Clinical Pathology* [*J. clin. Path.*] **8,** 229–236, Aug., 1955. 15 refs.

It has been shown that during the treatment of tuberculosis with a combination of streptomycin and PAS, resistance of the tubercle bacilli to streptomycin emerges more frequently when these organisms were resistant to PAS before treatment than when they were sensitive to it. In deciding on the most suitable chemotherapy for a patient with tuberculosis, therefore, the value of tests of the sensitivity of the infecting strain to PAS is clear. In the Medical Research Council trials in Great Britain such tests were carried out on "tween"-albumin medium, but American and French workers have claimed that tests on solid media are more reliable and easier to perform.

In the study here reported from the Postgraduate Medical School of London a comparison was therefore made between PAS-sensitivity tests carried out on tween–albumin (liquid) medium and on Löwenstein–Jensen (solid) medium. With the liquid medium the minimum concentration completely inhibiting growth was taken as the end-point; with the solid medium two end-points were used, one being the minimum concentration necessary to inhibit growth completely and the other the minimum concentration required to prevent the growth of 20 or more colonies.

Tests of 45 pre-treatment strains from patients who had received no previous chemotherapy showed that inhibitory concentrations were slightly lower in the liquid media. Examination of the 28-day readings on solid media showed that the "20-colony end-point" was, on the average, one concentration lower than the "no-growth end-point". The number of resistant strains that could be detected became larger as the incubation time increased. In the examination of 36 strains which had proved resistant to PAS the results in liquid and solid media were in agreement in only 21 instances; of the remainder, 7 yielded much higher results in the liquid medium and 8 on the solid medium. It was found that individual determinations of resistance were frequently very inaccurate. Decrease of resistance or reversion to sensitivity of some strains on storage, and significant differences in different batches of medium, add to these inaccuracies. On the whole the number of strains found to be resistant was very similar whether the tests were carried out on liquid or solid media. *E. G. Rees*

596. The Detection of Streptomycin Resistance in Tubercle Bacilli

S. M. STEWART. *Journal of Clinical Pathology* [*J. clin. Path.*] **8,** 237–241, Aug., 1955. 11 refs.

A method of detecting streptomycin resistance in *Mycobacterium tuberculosis*, which appears to be more sensitive than the routine method with "tween"–albumin medium, is described in this paper from the University of Edinburgh. The results were expressed as a resistance-ratio, this being the ratio of the minimum inhibitory concentration for the test organism to that for a control strain (H37Rv). Organisms were cultured on Löwenstein–Jensen medium and by the routine method for 4 weeks. A resistance ratio of 4 was regarded as indicating the emergence of a resistant strain.

Of 34 cultures appearing sensitive by the routine test but suspected to be resistant, all but one showed varying

degrees of resistance by the new test. All cultures which were found to be resistant by the routine test were also found to be resistant by the new test. It is suggested that failure to demonstrate streptomycin resistance in the liquid medium may be due to the presence of tween 80. *E. G. Rees*

597. **The Demonstration of Hitherto Unknown Pathogenic Factors in *Corynebacterium diphtheriae*; Their Significance in the Clinical Picture, Antitoxic Treatment, and Prophylaxis of Diphtheria.** (Der Nachweis bisher unbekannter Gifte des Corynebacterium diphtheriae, ihre Bedeutung für das klinische Bild der Erkrankung sowie die antitoxische Therapie und Impfprophylaxe)
H. NIGGEMEYER. *Annals paediatrici* [*Ann. paediat. (Basel)*] **185**, 1–60, July–Aug., 1955. 9 figs., bibliography.

When strains of the three major types of *Corynebacterium diphtheriae* were grown in a special broth medium in experiments carried out at the University Children's Clinic, Würzburg, 2 or 3 toxic substances were formed in addition to the classic diphtheria toxin. [For the complex composition of the broth medium the reader is referred to the original paper.] The first of these additional toxins is somewhat unstable in the presence of oxygen or unsuitable temperatures, but is rendered more stable by the addition of certain polysaccharides or hyaluronic acid or, in the case of Type-*gravis* strains, of salivary mucin or lecithin. It has a molecular weight of approximately 20,000 and its main toxic effect on rabbits and guinea-pigs is to cause rapid necrosis on injection into the skin. Some of the commercial preparations of antitoxin tested by the author were able to neutralize this necrotizing toxin, whereas others failed completely to do so. Certain strains of diphtheroid bacilli form a toxin with identical properties. The author considers this toxin to be an endotoxin and to be identical with the antigen described as " Substance B " by O'Meara (*J. Path. Bact.*, 1940, **51**, 317). The second additional toxin is a hyaluronidase formed by Type-*gravis* strains. [The author must have misread McClean's paper on this subject (*Lancet*, 1941, **1**, 595) since he quotes it in support of his findings, whereas in fact McClean was unable to isolate hyaluronidase from Type-*gravis* strains.] The third additional toxin is a haemolysin which, according to the author, may also be formed by a strain which he classifies as Type-*intermedius*. [So far as the abstracter is aware, haemolysis by Type-*intermedius* strains has not hitherto been demonstrated.]

The author considers that all three additional toxins play an important part in the clinical course of diphtheria. He readily concedes the overwhelming importance of the classic diphtheria toxin, but suggests that the inadequacy of antitoxin therapy in a proportion of cases may be due to the formation of the three additional toxins.

[The facts reported here have had to be extracted from a mass of largely irrelevant theorization. About half the paper consists of a somewhat biased survey of the literature.] *K. Zinnemann*

598. **The Detection of Botulinus Toxin in Artificially Contaminated Food Products with the Help of the Phagocytic Index Technique.** (Обнаружение ботулинового токсина, искусственно внесенного в пищевые продукты, при помощи определения фагоцитарного показателя)
V. R. SAVIN. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 44–50, No. 8, Aug., 1955.

It has been established by Minervin, Zhak, and Chervyakova that the toxin of *Clostridium botulinum*, the cause of botulism, suppresses the phagocytic activity of rabbit's blood, and that this antiphagocytic effect can be neutralized by specific antiserum. At the Odessa Medical Institute the author of the present paper has made an extensive study of the possible application of this phenomenon to the detection of botulinus toxin in meat, fish, and vegetable products. Extracts made from such products to which botulinus toxin A or B had been added were tested, with all appropriate controls, for the presence of botulinus toxin (1) by experiments on white mice *in vivo* and (2) by determining their effect on the phagocytic index of blood *in vitro*.

Extracts of canned products to which a weak botulinus toxin had been added in various dilutions caused a 2- to 12-fold reduction in the phagocytic index, enabling the presence of toxin to be detected up to a dilution of 1 in 100,000, whereas the extract had no effect *in vivo* when the toxin was added in dilutions greater than 1 in 25,000. Taking into consideration the necessity for a 5-fold dilution of the extract in performing the test *in vitro*, its sensitivity may be said to be 20 times greater than that of the test *in vivo*. Moreover, the result of the former test is available within 2 to 3 hours compared with at least 18 hours for the latter. The type diagnosis of the toxin present can be made by neutralization of the antiphagocytic effect by the specific antitoxin.

[If these findings are confirmed this technique may be of the greatest value for purposes of civil defence.]
K. Zinnemann

SEROLOGY AND IMMUNOLOGY

599. **A Complement Fixation Test for Poliomyelitis**
N. J. SCHMIDT and E. H. LENNETTE. *Journal of Experimental Medicine* [*J. exp. Med.*] **102**, 133–150, Aug. 1, 1955. 21 refs.

The authors describe a macroscopic (tube) complement-fixation test for poliomyelitis, developed in the laboratories of the California State Department of Health, the antigens being unconcentrated fluids harvested from monkey kidney tissue cultures infected with the 3 types of poliomyelitis virus. Serial twofold dilutions of each test serum were prepared with Kolmer saline solution, each dilution being dispensed into 3 series of tubes so that tests against each type of virus could be run concurrently. To each tube were added 0·2 ml. of antigen and 0·2 ml. of reconstituted lyophilized complement containing exactly 2 units and fixation allowed to proceed at 4° C. overnight. The tubes were then warmed in a

water-bath at 37° C. for 10 minutes and, after adding 0·5 ml. of sensitized sheep erythrocytes, incubated for 15 to 30 minutes, according to the time taken for control tubes without serum to clear. The titre recorded was the highest initial dilution of serum showing 3+ or 4+ fixation with the specific antigen. The potency of the antigens could not be increased by centrifugation, nor could the sensitivity of the test be increased by the use of larger volumes of antigen.

With paired or multiple serum specimens from patients with a clinical diagnosis of poliomyelitis a rise in complement-fixing antibody titre was observed in 18 out of 27 cases, while in 4 others there was a high stationary antibody titre. Of the remaining specimens, one gave high and equal antibody responses to 2 types of virus, 3 contained no detectable antibody (but the second specimen may have been taken too early after the onset of the illness for antibodies to have appeared), and one was from a patient who appeared not to have poliomyelitis. Heterotypic reactions were encountered, but caused no difficulty in interpreting homologous responses. Poliomyelitis virus was recovered from the stools of 15 of the patients and corresponded in type to that indicated by the serological findings.

Antibodies against the 3 types of poliomyelitis virus were not demonstrable, or only in low stationary titres, in paired specimens of serum from 12 patients with mumps, from 10 out of 11 patients with western equine encephalitis, and from 8 out of 10 patients with St. Louis encephalitis. A 4- to 8-fold rise in titre of antibodies against one or more of the 3 types of poliomyelitis virus occurred in the 3 remaining cases of encephalitis, but this may have been either an anamnestic response or due to a dual infection. *A. Ackroyd*

600. **Investigations on the Virus of Herpes Simplex. The Herpes Simplex Complement Fixation Test and Its Use in the Study of Herpes Antibodies.** [In English]
P. HALONEN. *Annales medicinae experimentalis et biologiae Fenniae* [*Ann. Med. exp. Biol. Fenn.*] Suppl. 9, **33**, 1–79, 1955. 1 fig., bibliography.

601. **A Study of Treponemal Immobilizing Antibodies in Spirochaetoses Other than the Treponematoses.** (Recherche des immobilisines antitréponémiques dans les spirochétoses autres que les tréponématoses]
J. RANQUE, R. DEPIEDS, and R. M. NICOLI. *Bulletin de la Société de pathologie exotique et de ses filiales* [*Bull. Soc. Path. exot.*] **48**, 326–328, 1955. 6 refs.

Biological false positive reactions to the serological tests for syphilis are commonly obtained in cases of the non-syphilitic spirochaetoses and in occasional cases of leishmaniasis and trypanosomiasis. The investigation reported here from the University of Marseilles was carried out to determine how far these conditions give rise to treponemal immobilizing antibodies active against *Treponema pallidum*. Blood from 2 patients infected with *Borrelia hispanica* was subjected to the treponemal immobilization (T.P.I.) test with the Nichols strain of *T. pallidum* with negative results. Blood from 21 guinea-pigs infected with the same organism also gave a negative reaction, but the survival time of the animals was only 13 days. In 7 cases of leptospirosis the T.P.I. reaction was negative; the classic serological tests gave negative reactions in 5 cases and dissociated responses in 2. Of 9 cases of tropical phagedenal ulcers due to Vincent's organisms, one gave a positive T.P.I. reaction, while of 8 cases of Vincent's angina, 2 gave a positive T.P.I. reaction. Of these 2 patients, one was a girl of 8 and the other a blood donor whose serological reactions had been consistently negative before his attack of Vincent's angina. However, in view of the positive T.P.I. reaction both patients were given anti-syphilitic treatment. *F. Hillman*

602. **Are Antitreponemal Reagins and Immobilizing Antibodies Elaborated in the Course of Clinical or Experimental Trypanosomiasis?** (Réagines et immobilisines antitréponémiques sont-elles élaborées au cours des trypanosomiases spontanées ou expérimentales ?)
J. RANQUE, R. DEPIEDS, and J. M. PHILIPON. *Bulletin de la Société de pathologie exotique et de ses filiales* [*Bull. Soc. Path. exot.*] **48**, 329–332, 1955. 5 refs.

Working at the University of Marseilles, the authors carried out the treponemal immobilization (T.P.I.) test and the Wassermann, Kolmer, Kahn, and Kline tests on sera from 32 patients with trypanosomiasis acquired naturally in Africa. In 8 cases positive results were obtained with all tests and in 29 all the reactions were negative. In the remaining 3 cases the T.P.I. reaction was negative and the other tests gave equivocal results. The proportion of positive reactions in this series is much lower than the proportion usually quoted in the literature.

Among 7 patients experimentally infected with *Trypanosoma gambiense* for the treatment of mental disease not a single positive T.P.I. reaction was found, and only in one case was the Kolmer reaction temporarily positive. Experimental infection of 35 guinea-pigs with the same organism gave rise to transitory positive Kahn, Kolmer, and Kline reactions only, while sera from 24 guinea-pigs infected with *T. brucei* gave negative T.P.I. reactions 15 days after infection. In 24 rats and 36 guinea-pigs infected with *T. equiperdum* the reactions to the standard tests for syphilis became positive, but were negative again 4 days later. However, the strain of *T. equiperdum* was so virulent that the average survival of the animals was only 12 days, which may have been too short a period to allow of the production of reagins and immobilizing antibodies, although it was long enough for changes demonstrable by electrophoresis to occur in the serum gamma globulins.

The authors conclude from this evidence that the trypanosomiases *per se* do not give rise to a positive T.P.I. reaction and that this test should enable a decision to be reached in cases where the diagnosis is in doubt. But when trypanosomiasis is accompanied by persistent positive serological reactions for syphilis it must be considered to be associated with treponemal infection. Such a case will often fail to respond to antitrypanosomal treatment, but will improve when antitreponemal treatment is substituted. *F. Hillman*

Pharmacology

603. Comparative Efficacy of Hypnotics. A Self-controlled, Self-recorded Clinical Trial in Neurotic Patients

E. H. HARE. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **9**, 140–146, July, 1955. 10 refs.

An account is given of the technique of a comparative trial of the efficacy of various hypnotics carried out at Barrow Hospital, Bristol, on 30 female patients with insomnia due to neurosis, and of the internal and external checks used to ensure the reliability of the patient's recorded opinion of each night's sleep. The former check was provided by the night nurse, and the latter by giving the same drug in differently coloured capsules on different occasions. A system of scoring was used in conjunction with a standard form on which the patient recorded her impression of the quality of sleep obtained, including the time taken to get off to sleep and her feelings on waking. The nurse's record was similarly marked in relation to the duration of sleep and restlessness, but the condition of the patient on waking was regarded as purely subjective and this part of the patient's score was omitted for purposes of correlation. Adjustments to the scores were made for any unrelated circumstance affecting sleep, such as pain or a disturbance in the ward. [The method appears suitable for this type of investigation.]

The following drugs were tested in the doses stated, and are listed in decreasing order of effectiveness: butobarbitone, 3 grains (0·2 g.); carbromal, 12 grains (0·78 g.) and sodium butobarbitone, 3 grains (roughly equally effective); methylpentynol, 0·5 g.; and a placebo. *P. Mestitz*

604. Spirometry in Assessment of Analgesia after Abdominal Surgery. A Method of Comparing Analgesic Drugs

P. R. BROMAGE. *British Medical Journal* [*Brit. med. J.*] **2**, 589–593, Sept. 3, 1955. 5 figs., 12 refs.

The objective assessment of the efficacy of pain-relieving drugs has always been a problem, and the present author, writing from the Chichester and Portsmouth Hospital Groups, describes yet another method of assessing the relief of pain in the 48 hours following upper abdominal operations. After such operations there is a reduction in vital capacity which is [presumed to be] due almost entirely to pain. The degree of restoration of the vital capacity towards normal after administration of analgesic drugs or after pain-relieving procedures has been taken as a quantitative index of the efficacy of the drugs or procedures.

Vital capacity, taken as the average of the 3 largest respirations out of 4, was measured with the patient in the supine position, a Benedict–Roth recording spirometer containing air being used. Base-line readings of "pain vital capacity" were taken after the anaesthetic had worn off, and before each analgesic was given. In 20 patients serial readings were taken after each drug had been administered, the order of administration varying. Epidural injection of 0·8% lignocaine ("xylocaine") restored the vital capacity an average of 80% towards normal (range 50% to 138%); intravenous injection of pethidine (dosage 1·4 mg. per kg. body weight) restored it 13% (−2% to 37%); methadone intravenously (0·14 mg. per kg. body weight) 35% (9% to 101%), and 0·5% lignocaine by intravenous drip (400 to 500 mg. in 40 to 60 minutes) 23% (7% to 68%).

The limitations of the method are freely admitted by the author. It is applicable only to wound pain after upper abdominal operations; central depression—for example, by intravenous pethidine or lignocaine—leads to poor ventilatory performance despite effective analgesia. On the other hand, epidural block results in a fall in systemic blood pressure and consequent improved ventilation in patients with left heart strain, and an erroneously high index of analgesic efficacy. The method is of no value if the drug under test has a respiratory stimulant action. *T. B. Begg*

605. The Effect of Nitroglycerine upon the Cardiovascular System

F. L. ELDRIDGE, H. N. HULTGREN, P. STEWART, and D. PROCTOR. *Stanford Medical Bulletin* [*Stanford med. Bull.*] **13**, 273–283, May, 1955. 4 figs., 34 refs.

At Stanford University School of Medicine, San Francisco, the authors investigated the mechanism of the beneficial effect of nitroglycerin on angina pectoris. The relief of pain may be due to two possible factors, namely, coronary vasodilatation and a reduction in cardiac work. The latter might be brought about by peripheral vasodilatation producing a fall in blood pressure without an elevation of the cardiac output, the work done by the heart being a product of its output and the arterial pressure. Although it has repeatedly been shown that nitroglycerin increases the coronary blood flow in animals, this effect has never been demonstrated in man.

Evidence of the hypotensive effect of the drug in man has never been obtained from erect, exercising subjects, while there are conflicting views on its action on cardiac output.

In an attempt to obtain more exact information on the mode of action of the drug 22 patients were studied during routine cardiac catheterization; 2 were healthy and the rest had congenital or rheumatic heart disease, though none was suffering from cardiac failure. Five of the patients were anaesthetized throughout the investigation. Nitroglycerin was given by mouth or intravenously in doses averaging 0·018 mg. per kg. body weight. The blood pressure and pulse rate were recorded

from the femoral or brachial artery, and the mean right auricular pressure from the cardiac catheter; the oxygen content of venous and arterial blood was measured, and oxygen consumption was determined by collection of the expired air in a Tissot apparatus. Analysis of results showed an average decrease in cardiac work of 13% as a result of administration of nitroglycerin. The authors believe that the reduction of cardiac work which they were able to demonstrate may play as large a part in the relief of angina as the effect on the coronary vessels themselves. To support this hypothesis they cite the fact that hexamethonium may improve angina in cases of hypertension.

In a further experiment the blood pressure of 10 healthy subjects aged 21 to 26 was recorded at 2-minute intervals during standard exercise. When a constant level of blood pressure and heart rate had been reached 0·4 mg. of nitroglycerin was given sublingually and exercise continued for 6 to 8 minutes, the blood pressure being recorded as before. It was found that the systolic pressure rose by an average of 42·2 mm. Hg during exercise and fell on giving nitroglycerin by an average of 26·5 mm. Hg, the heart rate increasing from 128 to 145·2 beats per minute on average.

[This interesting and iconoclastic study serves as a reminder that there are still many accepted notions in medicine which merit reinvestigation by modern methods.]

G. S. Crockett

606. **Pharmacologic and Antiarrhythmic Actions of Ambonestyl (2-Diethylaminoethyl*iso*nicotinamide) in Man. Preliminary Report**

B. B. Clark and B. Etsten. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 217–223, Aug. 11, 1955. 6 figs., 11 refs.

"Ambonestyl" is closely related chemically to procainamide. It has been shown to be as effective as procainamide or quinidine in controlling cardiac arrhythmias in animals without depressing conduction, and as it has little hypotensive, ganglion-blocking, or local anaesthetic properties it should have a wider margin of safety. At the New England Center Hospital (Tufts University School of Medicine), Boston, the authors have studied the effects of ambonestyl in man, the subjects being 8 healthy controls and 8 patients with cardiac arrhythmia The arrhythmias were ventricular in all but one, a case of atrial premature beats, and comprised bigeminal rhythm (3 cases), premature ventricular contractions (3 cases), and partial atrioventricular block (one case).

In normal subjects after the intravenous injection of ambonestyl in doses up to a total of 750 mg. there was a transient depression of the T wave in the electrocardiogram, an increase in the heart rate, and a transient fall in blood pressure, but no change in cardiac output; the injection caused a subjective sensation of warmth spreading over the body.

In 5 cases the arrhythmia arose during or after anaesthesia with thiopentone, nitrous oxide, or cyclopropane. Ambonestyl was given in doses of 0·5 to 3·5 g. and effectively suppressed premature ventricular contractions and bigeminal rhythm in all cases. With smaller doses the arrhythmia was only temporarily suppressed and tended to recur later, but after larger doses normal rhythm was maintained for longer periods. Doses of 0·5 g. were given intravenously at 10-minute intervals, and no undesirable side-effects were observed even when the total reached 3 g. In 2 further cases the drug was of value in controlling ventricular ectopic activity and in maintaining better cardiac function during operative procedures on the heart. No response was observed in the case of atrial premature beats.

The authors conclude that further clinical trial of ambonestyl is justified.

R. Wien

607. **The Demonstration and Evaluation of the "Spreading Effect" by the Measurement of Intrinsic Tissue Pressure.** (Über die Brauchbarkeit der Gewebsinnendruckmessung für Nachweis und quantitative Erfassung des "Spreading-Effektes")

H. J. Heite and M. Karst. *Archiv für klinische und experimentelle Dermatologie* [*Arch. klin. exp. Derm.*] **201**, 201–217, 1955. 7 figs., bibliography.

Current methods of measuring the spreading effect of hyaluronidase are inaccurate, being based on the determination either of the rate of diffusion of dyes of complex molecular structure injected into the skin or of the permeability of the blood vessels to substances of low molecular weight. The observation of Lenstrup (*Acta pharmacol.* (*Kbh.*), 1951, **7**, 143) that the pressure needed to maintain the flow of a subcutaneous infusion of saline in rabbits at a constant rate was reduced by hyaluronidase and that the rate of flow was increased by hyaluronidase when the pressure remained constant was confirmed by the present authors at the Philipps University, Marburg. As a means of measuring the spreading effect, however, this method was discarded as it was found difficult to keep the pressure or rate of flow steady for any length of time, while slight differences of position of the needle in the tissues affected the results.

Eventually a reliable technique giving reproducible results in guinea-pigs was evolved, based on the measurement of the pressure necessary to inject 0·2 ml. of saline through an intradermal cannula. It was found that the effect of the injected fluid had worn off within 60 minutes, a reading similar to the first being obtained on repeating the injection after that interval. An injection of hyaluronidase caused the pressure reading to fall to half the initial value within 2 hours, but its effect lasted approximately 12 hours only, which is a much shorter period of activity than that suggested by different techniques. Moreover, ACTH (corticotrophin) and cortisone, which are shown by other methods to minimize the spreading effect of hyaluronidase, did not prevent its action on tissue pressure.

It would appear, therefore, that the mechanism of the effect of hyaluronidase on tissue pressure differs from that of its effect on diffusion and permeability. This is further suggested by the finding that the tissue pressure was unchanged after intravenous injection of hyaluronidase in doses sufficient to cause an increase in the rate of fluid resorption from intradermal weals.

G. W. Csonka

Chemotherapy

608. **Clinical Evaluation of Puromycin in Human Neoplastic Disease**
J. C. WRIGHT, V. B. DOLGOPOL, M. LOGAN, A. PRIGOT, and L. T. WRIGHT. *Archives of Internal Medicine* [*Arch. intern. Med.*] **96**, 61–77, July, 1955. 5 figs., 10 refs.

Since puromycin, an antibiotic obtained from *Streptomyces albo-niger*, has appreciable inhibitory activity against certain tumours in animals, it was tried at Harlem Hospital, New York, in the treatment of 51 patients suffering from advanced, disseminated, neoplastic disease, 250 to 750 mg. being given by mouth daily. There was slight temporary regression of the tumour in 15 patients treated for 21 days or more, but no change was observed in the progressive downhill course of the disease. Side-effects included nausea, vomiting, and diarrhoea, but these subsided promptly on cessation of treatment. *G. Calcutt*

609. **An Evaluation of Potassium *para*Aminosalicylate**
S. M. CHERNISH and F. B. PECK. *Antibiotic Medicine* [*Antibiot. Med.*] **1**, 377–381, July, 1955. 3 refs.

Since *para*aminosalicylic acid (PAS) and its sodium salt give rise to troublesome gastric disturbances in a large proportion of patients, the present authors, at the General Hospital, Indianapolis, tried the potassium salt in the treatment of 102 patients with pulmonary tuberculosis. In a preliminary investigation it was found that the blood level of PAS was higher after ingestion of the potassium salt than after ingestion of a corresponding dose of the sodium salt; moreover there were no indications of undue potassium retention. Of the 102 patients given potassium PAS, 32 who had previously been intolerant of other forms of the drug found it satisfactory and 6 remained intolerant of all forms. Another trial indicated that there was little reduction in the incidence of gastric disturbances if the daily dose of PAS exceeded 12 g. *J. Robertson Sinton*

610. **Tuberculostatic Activity of 2-Pyridyl-(4)-1:3:4-oxdiazolon-(5), Its *p*-Aminosalicylate and Other Related Substances**
H. BRODHAGE and A. E. W. SMITH. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **49**, 185–197, July, 1955. 3 figs., 28 refs.

The treatment of tuberculosis with isoniazid alone leads to the early appearance of bacterial resistance, and to prevent or delay this as long as possible the drug is now commonly used alternately or in combination with one or even two other chemotherapeutic agents. The appearance of resistance might also be delayed if a higher blood level of isoniazid could be achieved. The activity of the drug *in vivo* and *in vitro* is greatly reduced by its acetylation during the normal process of metabolism and excretion, and it therefore appeared desirable to synthesize and test derivatives of isoniazid which might be less readily acetylated.

The present paper from the Lucerne Cantonal Hospital and the Geistlich Research Laboratories, Wolhusen, briefly reports the results of tests carried out *in vitro* and *in vivo* on 7 such substances, as a result of which an eighth compound was synthesized by allowing isoniazid to react with phosgene in the presence of a solvent. This substance, 2-pyridyl-(4)-1:3:4-oxdiazolone (Compound I) and the complex which it forms with PAS (Compound II) had considerably greater tuberculostatic activity than any of the others and were subjected to more extensive tests. Both compounds had a weaker tuberculostatic effect *in vitro* than isoniazid, but in guinea-pigs that of Compound I was about the same as that of isoniazid and that of Compound II equal to that of the *p*-aminosalicylate of isoniazid. This may be explained by the greater chemical stability of the new compound. The toxicity of both compounds was very much less than that of isoniazid in the guinea-pig, rabbit, mouse, and rat. Compound II was active *in vitro* against isoniazid-resistant strains of *Mycobacterium tuberculosis*, while subculture of *M. tuberculosis* in the presence of either compound led to the development of resistance far more slowly than is the case with isoniazid. Clinical trials of Compound II have been carried out on over 160 patients, the dose used being between 600 and 2,500 mg. daily for 2 to 12 months. The preparation was well tolerated and so far the results have been promising, early cases reacting very well, while in 2 rapidly deteriorating cases which had not responded to any other form of medication there was a spectacular response to Compound II which " can be described as life saving ". *E. Forrai*

611. **The Management of Hypersensitivity Reactions to Streptomycin and PAS**
A. SANDLER. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **49**, 231–241, July, 1955. 14 refs.

Clinical details are given in this paper from the University of Edinburgh of 19 cases of hypersensitivity to streptomycin or PAS, or both, in patients receiving these drugs and of one case of dermatitis occurring in a staff nurse in daily contact with streptomycin. There were 9 cases of streptomycin hypersensitivity, one being the case of contact dermatitis mentioned above and 3 being probably cases of hypersensitivity to the sulphate radicle only. Hypersensitivity to PAS occurred in 6 cases, with jaundice in 2 of them. Combined streptomycin and PAS hypersensitivity occurred in 5 cases.

Desensitization with progressively increasing doses of the drug concerned was successfully carried out in 17 cases, in one of which cortisone was given at the same time owing to the presence of exfoliative dermatitis. In the remaining 3 cases the reactions ceased on substituting streptomycin calcium chloride for streptomycin sulphate. *Kenneth Marsh*

Infectious Diseases

612. **Further Experience in the Treatment of Scarlet Fever with Penicillin in Oil. The Question of Early Discharge.** (Weitere Behandlungsergebnisse mit öligem Depot-Penicillin beim Scharlach. Zugleich ein Beitrag zur Frage der Frühentlassung)

J. STOERMER. *Archiv für Kinderheilkunde* [*Arch. Kinderheilk.*] **151**, 36–43, 1955. 29 refs.

The results of observation of a series of 300 children after treatment at the University Children's Clinic, Göttingen, for scarlet fever (haemolytic streptococci having been recovered from the throat in 79% of cases) support the view that with routine treatment with penicillin combined with efficient measures of isolation in hospital early discharge may safely be permitted. A depot preparation of procaine penicillin in oil was used in these cases and was considered satisfactory. Injections of 1, 1·2, and 1·5 mega units were given to children under 4, between 4 and 8, and over 8 respectively, generally on the 4th day of illness, and for children over 8 a second injection (900,000 units) on the 7th day, on which day all the children were bathed, given a complete change of clothing, and transferred to clean cubicles, generally being discharged on the 11th day of illness. Thus treated patients were in association in the ward with fresh cases for at most 3 days.

While some complications were observed both in hospital and after discharge, there was no instance of spread of infection on return home, and no child caught the disease for a second time. It is pointed out that early discharge reduces the risk of reinfection and superinfection.

R. Crawford

613. **Epidemiology of RI (RI-67) Group Respiratory Virus Infections in Recruit Populations**

M. R. HILLEMAN, J. H. WERNER, H. E. DASCOMB, R. L. BUTLER, and M. T. STEWART. *American Journal of Hygiene* [*Amer. J. Hyg.*] **62**, 29–42, July, 1955. 3 figs., 13 refs.

The incidence of acute respiratory illness among groups of recruits at the U.S. Army Hospital, Fort Dix, New Jersey, and the results of serological tests for the RI group of viruses are reported.

In the first group of 209 recruits who were assembled for training at the end of January, 1954, there was an epidemic of acute respiratory illness with a peak in the second week after the men were brought together. Two strains of the RI group of viruses predominated. Initially the complement-fixing (C.F.) antibody titre was low, but in 77% of the subjects a fourfold increase was observed in the 6 weeks following the peak of the illness; a similar increase in antibody titre was found in recruits who were mildly ill or had no apparent infection. This rise in C.F. antibody titre was accompanied by a similar rise in neutralizing antibody titre against one or both strains of the virus. In the second group of 210 recruits, who were inducted in July, 1954, there was a much lower incidence of respiratory disease; only 10% of these showed a significant rise in antibody titre to the RI group of viruses.

Generally the respiratory illness was associated with an increase in antibody titre to the viruses; the C.F. antibody present initially did not appear to exert a protective effect. Antibody titres reached a peak in 2 to 4 weeks, declining gradually over a year.

G. C. R. Morris

614. **Tetracycline in the Treatment of Infectious Hepatitis**

T. W. WODRASKA. *Antibiotic Medicine* [*Antibiot. Med.*] **1**, 327–333, June, 1955. 5 figs., 11 refs.

Tetracycline was tried in the treatment of cases of infective hepatitis occurring during an epidemic of the disease at Rockland State Hospital, Orangeburg, New York. Of a total of 60 patients, 45 received the drug by mouth in a dosage of 1 to 1·5 g. daily for 10 to 12 days; the remaining 15, who served as controls, received no treatment other than rest in bed and a high-calorie, high-carbohydrate diet. In 36 of the 45 treated patients the illness lasted no more than 1 to 2 weeks, whereas in the control group the average duration of the illness was 5 to 8 weeks.

An attempt was made during the epidemic to limit the spread of the disease by isolation of patients and inoculation of contacts with gamma globulin. The author concludes from his experience that this prophylactic measure is effective if introduced " early after the outbreak and on a sufficiently broad scale ".

G. C. R. Morris

615. **The Mumps Skin Test and Complement Fixation Test as a Diagnostic Aid in Sarcoidosis**

E. L. QUINN, D. C. BUNCH, and E. YAGLE. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **24**, 595–598, June, 1955. 7 refs.

Immunological reactions indicative of previous mumps infection occur in 75 to 85% of adults, and in 93% of cases in which the complement-fixation test gives a positive reaction the skin reaction to mumps virus is also positive. In sarcoidosis, however, this correlation appears to be upset. In all of 7 consecutive cases examined at the Henry Ford Hospital, Detroit, the complement-fixation reaction for mumps was positive, yet the skin reaction was negative in all but one. In contrast, only one of 8 patients suspected of sarcoidosis, but in whom the diagnosis was not substantiated on subsequent study, gave a negative skin reaction with a positive complement-fixation reaction.

The authors point out that before the diagnostic value of these findings can be judged the correlation between the two reactions must be studied in diseases other than sarcoidosis in which there is a disturbance of skin anergy—for instance, in Hodgkin's disease.

E. W. Prosser Thomas

Tuberculosis

PROPHYLAXIS

616. **The Protection of the Children of Tuberculous Parents.** (La protection de l'enfant de parents tuberculeux)
M. GRAFFAR and M. ASIEL. *Acta tuberculosea Belgica* [*Acta tuberc. belg.*] **46**, 182–206, June, 1955. 16 refs.

The first part of this paper reports the results of an investigation into the effect on morbidity from tuberculosis in children of removing them from contact with their tuberculous parents. A total of 250 children from 101 families were studied, 111 having been kept away from home for varying periods, while the remainder had stayed at home. The results were poor because children were often not removed in time, or returned home before the danger of infection had passed.

The second part of the paper describes observations on 140 children of tuberculous families, 85 of whom had been vaccinated with B.C.G. at birth, while the remaining 55 had not been vaccinated. The study was retrospective, but care was taken to ensure that only those children of similar age and social background were compared. Tuberculous lesions of all kinds were observed to be 4 times more frequent among the control group than the vaccinated group. Serious tuberculous lesions were about 7 times more frequent in the control group, and 9% of this group developed miliary tuberculosis or meningitis, resulting in 2 deaths.

The authors recommend that when a case of tuberculosis occurs in a family all children who may be at risk should receive B.C.G. Similarly, any child born into such a family should receive B.C.G. at once. After vaccination and until allergy is established the children should be protected from contact with the disease so far as possible, either at home or by removal to a suitable institution. *T. M. Pollock*

617. **The Investigation of Tuberculous Allergy by Means of Intradermal B.C.G.** (Recherche de l'allergie tuberculeuse par BCG-réaction intradermique)
R. DASSONVILLE. *Bulletin de l'Académie nationale de médecine* [*Bull. Acad. nat. Méd.* (*Paris*)] **139**, 238–241, April 19, 1955. 8 refs.

This paper describes an attempt to determine whether the intradermal B.C.G. test is more suitable for the assessment of results of B.C.G. vaccination than the tuberculin test in circumstances where opportunities for reading the reaction occur only at weekly intervals. The tests were carried out 2 months after vaccination on 43 boys aged 12 to 13 years. All were given a tuberculin test, 21 were given a similar test using a suspension of B.C.G. in a concentration of 75 mg. per ml. killed by heating to 70° C. for one hour, the dose being approximately 1/200 mg., and the remaining 22 were given the same test using living B.C.G. The reactions were read on the 4th, 6th, 8th, 15th, and 29th days.

The reaction to the tuberculin test consisted in a raised red area varying between 2 and 8 mm. in diameter. It began to regress after the 6th day and had practically disappeared by the 15th day. The intradermal inoculation of killed B.C.G. resulted in an area of infiltration with, in 3 cases, a central vesicle appearing on the 8th day which became encrusted and desquamated after the 2nd week. The infiltrated area was similar in extent to that of the tuberculin reaction; as it regressed its colour changed from red to a shade of purple. The reaction declined more gradually than that of the tuberculin test, and was still visible after 4 weeks. The reaction to living B.C.G. resembled that to killed B.C.G. but was more intense. The area of infiltration was between 4 and 12 mm. in diameter and in 8 cases there was a vesicular reaction.

It is concluded that the B.C.G. test is a suitable post-vaccination test and that it is best carried out with living B.C.G. *T. M. Pollock*

618. **The So-called Intensive Method of Vaccination with B.C.G. by the Oral Route.** (Sur l'usage de la vaccination BCG dite intensive par voie buccale)
E. BERNARD, J. CROS-DECAM, —. LE JOUBIOUX, and —. BOUVRAIN. *Bulletin de l'Académie nationale de médecine* [*Bull. Acad. nat. Méd.* (*Paris*)] **139**, 379–383, July 5, 1955.

This paper describes the results in 119 infants of vaccination with B.C.G. given by mouth in large doses. Both dried and fresh vaccines from the Pasteur Institute were used, the dosage varying between a single dose of 50 mg. and 4 doses of 100 mg. at intervals of 7 to 16 days. Two doses, of 50 mg. for infants under 6 months and of 75 mg. for those over 6 months, appeared to give satisfactory results. In 72 cases 1/100 mg. of B.C.G. killed by heat was injected intradermally at the time of vaccination; some weeks later an allergic reaction appeared at the site of inoculation in each case.

Tuberculin tests were carried out by various techniques in all cases, a positive result being usually observed between 6 and 8 weeks after vaccination, the range being 4 to 12 weeks. Delay in the development of allergy was longest and the intensity of the reaction least in those given a single dose of 50 or 75 mg.; maximum allergy was produced with two doses, there being no increase in the intensity of the reaction when further doses were given.

Only 6 of the infants failed to become allergic to tuberculin after vaccination; in 3 of these cases only a single dose of 50 mg. had been given. No differences were observed between the results obtained with fresh and dried vaccine. No complications of this method of vaccination were noted. *T. M. Pollock*

RESPIRATORY TUBERCULOSIS

619. The Role of Bronchoscopy in Tuberculosis of Infancy and Childhood

H. J. RUBIN and M. S. HARRIS. *Diseases of the Chest* [*Dis. Chest*] **28**, 188–195, Aug., 1955. 5 refs.

The value of bronchoscopy in tuberculosis in infants and young children was studied at the County General Hospital, Los Angeles. Between September, 1951, and December, 1953, a total of 37 children under the age of 4 years suffering from tuberculous endothoracic disease were subjected to bronchoscopy under open ether anaesthesia; this procedure permitted adequate inspection of the bronchial tree with a minimum of trauma and, because instrumentation was gentle, did not cause post-bronchoscopic subglottic oedema. In 12 of the patients the bronchograms were abnormal, endobronchial granulomata being present in 7, marked compression of the air passages by enlarged lymph nodes in 4, and severe inflammatory bronchial stenosis in one patient.

It was not possible to distinguish these 12 patients from the remaining 25 on clinical and radiological grounds, but in retrospect it was noted that some of the 12 did not respond satisfactorily to routine treatment with streptomycin, PAS, and isoniazid until granulomatous tissue had been removed.

The authors emphasize the importance of relieving these endobronchial lesions if subsequent bronchiectasis is to be avoided [but the number of patients is too small and the follow-up period too short for any statistical evaluation]. *R. M. Todd*

620. A Clinico-pathological Study of Atelectasis in Pulmonary Tuberculosis

L. J. TEMPLE. *Thorax* [*Thorax*] **10**, 220–228, Sept., 1955. 18 figs., 22 refs.

This report from the University of Liverpool is based on the findings in 125 lungs or portions of lung removed from patients with pulmonary tuberculosis in whom atelectasis had been diagnosed before operation. Each specimen was distended with formalin to fix it in its original size, embedded in gelatin, and sliced as a whole into sections 500 μ thick, small portions being taken at appropriate points for microscopical examination. In this way a picture of the entire anatomy of the specimen was obtained.

From the results of this investigation the author concludes that a distinction must be made on pathological grounds between two types of atelectasis in pulmonary tuberculosis. (1) Massive collapse of a lung or lobe as a result of bronchial stricture, with bronchiectasis and fibrosis distal to the stricture. The lung in such specimens often shows a good healing response, and the danger lies in the spill-over of trapped caseous material into healthy lung tissue. (2) Atelectasis following collapse therapy for circumscribed parenchymal lesions. In these cases atelectatic lung tissue surrounds the lesion; the collapse is never segmental in distribution and is due not to bronchial involvement, but to compression of the lung against the hard, unyielding tuberculous lesion. Such a lesion, whether solid or cavitated, is active, and spread soon takes place to the surrounding collapsed tissue. The development during collapse therapy of small areas of atelectasis related to tuberculous lesions is therefore a danger signal indicating actively spreading disease. *P. Mestitz*

621. The Importance and Incidence of Distal Bronchial Involvement in Pulmonary Tuberculosis. (De l'importance et de la fréquence de la tuberculose bronchique distale au cours de la tuberculose pulmonaire)

J. GIRARD, J. P. GRILLIAT, A. SIMON, A. PETERS, and J. LORRAIN. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **19**, 331–350, 1955. 8 figs., 22 refs.

For the past few years the authors have carried out bronchography, using a " lipiodol " spray for coating the bronchial tree, to detect any changes in the bronchi in a large number of cases of tuberculosis; the first 200 female in-patients in whom bilateral filling was achieved are the subjects of this paper.

Bronchial involvement was found in 170 cases (85%) mainly in the shape of moniliform dilatation, but saccular and cylindrical bronchiectasis also occurred. Complete bronchial disorganization, without stenosis of the main bronchus, was present when parenchymatous disease was sufficiently extensive. The lesions were commonest in the upper lobes and segments previously invaded by tuberculous disease, noteworthy exceptions being the frequent involvement of the lingula of the left lung and the sparing of the right middle lobe. Fibrotic disease was usually found to be associated with bronchial damage. The investigation of recent infiltrations, however, was unsatisfactory, probably, the authors suggest, because the presence of oedema and exudate interfered with proper filling with lipiodol. Cavities were sometimes outlined, but more commonly there was no filling, in spite of the fact that associated bronchi were usually extensively involved. In a small number of cases basal bronchiectasis was found, although no parenchymatous disease had been observed radiologically. In some of the cases in which resection was carried out histological examination revealed a caseating process involving all layers of the bronchial wall. The authors regard this process, rather than stasis or endobronchial stenosis, as the chief aetiological factor in the causation of bronchial dilatation in cases of pulmonary tuberculosis.

J. Robertson Sinton

622. Hepatic Damage in Chronic Pulmonary Tuberculosis

B. BAN. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 71–90, July, 1955. 22 figs., 28 refs.

Because hepatic damage is a frequent finding at necropsy in cases of pulmonary tuberculosis, liver function tests were carried out and liver biopsy specimens were examined in 60 cases of pulmonary tuberculosis and, for control purposes, in 34 cases of chronic non-tuberculous pulmonary infection at the Tuberculosis Clinic, Delhi. In the non-tuberculous group the hepatic

damage appeared to be incidental and minor in degree; in the patients with pulmonary tuberculosis, whether treated or untreated, the structural changes in the liver were greater and the incidence was much higher than in the non-tuberculous group.

The results of three or more liver function tests were abnormal in only 5 of the 34 patients with non-tuberculous infection, and histological changes were observed in liver biopsy material in only 6 (out of 33). In 45 of the 60 patients with pulmonary tuberculosis the results of the thymol turbidity and cephalin–cholesterol flocculation tests were abnormal, and in 51 there was an increase in " bromsulphalein " retention with disturbance of the albumin:globulin ratio. Histological examination of biopsy specimens revealed classic miliary tubercles in the liver in 5 of the 60 patients, although there was no evidence, on clinical examination, of miliary tuberculosis; in a further 7 cases there were tubercle-like lesions in the liver, again without clinical manifestations of miliary tuberculosis. Fatty degeneration, necrosis, regeneration of liver cells, portal sclerosis, and amyloid deposits were observed in 45 cases. The author found that there was a correlation between the degrees of structural and functional change in the liver. The nutrition of the patients did not appear to play any part in the production of these changes, which were not related to the duration of the tuberculosis or influenced by treatment.

The author considers that since these structural changes were not found in the patients with non-tuberculous infection they were " presumably the result of the toxicity of the pulmonary tuberculosis itself ".

Kenneth M. A. Perry

623. **Experience with Streptomycyclidene *iso*Nicotinyl Hydrazine Sulfate in the Treatment of Mentally Sick Tuberculous Patients**

R. ROSENFELD. *Antibiotic Medicine* [*Antibiot. Med.*] 1, 446–449, Aug., 1955. 4 refs.

The results of the treatment of 51 mental patients, including 28 schizophrenics, suffering from pulmonary tuberculosis at the Oregon State Hospital with streptomycyclidene *iso*nicotinyl hydrazine sulphate (S.I.S.) for 2 to 16 months are compared with those obtained in 51 cases treated conventionally with isoniazid, alone or with PAS or streptomycin or both.

Five of the former group underwent pulmonary resection in addition, while 2 of the latter were treated with artificial pneumothorax and 3 with pneumoperitoneum and phrenic crush. The dose of S.I.S. was 1 ampoule injected intramuscularly daily for 1 to 3 months and then twice weekly, each ampoule containing 1 g. of streptomycin and 236 mg. of isoniazid in chemical combination. On intervening days 200 mg. of isoniazid was given by mouth or 150 mg. intramuscularly. The mental condition of the patients after treatment with S.I.S. was unchanged in 28 cases, improved in 17, and worse in 6, while none of the control subjects deteriorated and 20 showed some improvement.

The results of treatment in the two groups, as judged from weight changes and x-ray and bacteriological findings, were similar. Side-effects occurred in 12 of the patients given S.I.S., 9 of whom developed a transient skin rash while 3 complained of dizziness. Bacterial resistance (to streptomycin only) developed in one case as a result of S.I.S. treatment.

The author concludes that there was little difference between the results obtained in the two groups. The chief advantage of using S.I.S. was that more accurate control of dosage could be obtained in uncooperative mental patients. [The saving of nursing time in hard-pressed units would also seem to be a point in favour of this compound. The numbers of patients studied were too small, however, for any hard and fast conclusions to be drawn concerning its efficacy.] *I. M. Librach*

624. **Reduced Sensitivity to Isoniazid in Patients with Untreated Pulmonary Tuberculosis.** (Herabgesetzte Empfindlichkeit gegen INH bei Patienten mit unvorbehandelter Lungentuberkulose)

U. BALDAMUS and U. PONICK. *Tuberkulosearzt* [*Tuberkulosearzt*] 9, 476–482, Aug., 1955. 1 fig., 8 refs.

Between January, 1953, and December, 1954, the sensitivity of 500 strains of *Mycobacterium tuberculosis* to thiacetazone, PAS, streptomycin, and isoniazid was tested at the Heim Sanatorium, Berlin. Of these, 374 were sensitive to all four chemotherapeutic agents; of the remainder, 114 showed reduced sensitivity to isoniazid only, 3 to both isoniazid and PAS, 4 to isoniazid and streptomycin, one to isoniazid and thiacetazone, and 2 to isoniazid, PAS, and streptomycin, while one strain showed reduced sensitivity to PAS and one to thiacetazone only. Five of the isoniazid-resistant strains were isolated from patients who had not received any previous chemotherapy. The view is expressed, however, that these were derived by cross-infection from patients who had been treated with isoniazid, and did not represent naturally occurring resistant strains.

H. F. Reichenfeld

625. **The Prevalence of Streptomycin- and Isoniazid-resistant Strains of *Mycobacterium tuberculosis* in Patients with Newly Discovered and Untreated Active Pulmonary Tuberculosis**

A. D. CHAVES, A. B. ROBINS, H. ABELES, L. R. PEIZER, G. DANGLER, and D. WIDELOCK. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] 72, 143–150, Aug., 1955. 5 refs.

The study reported was carried out by the New York City Department of Health between July, 1953, and January, 1955, when samples of sputum were examined from 610 patients with newly diagnosed pulmonary tuberculosis and from 288 with recently reactivated disease, none of whom had ever received antimicrobial treatment, the specimen being received in each case within 6 months of the date of diagnosis of active or reactivated infection. Each sample was digested with trisodium phosphate and the concentrate cultured on slopes of drug-free agar medium and of media containing 10 μg., 100 μg., and 1,000 μg. of streptomycin per ml. and 0·1 μg., 1 μg., and 5 μg. of isoniazid per ml.

Growth on the drug-free medium was observed in 285 of the newly diagnosed and 100 of the reactivated cases,

a total of 43%. [This remarkably low proportion of positive cultures may be attributable to the digestion with trisodium phosphate, which is known to be more lethal to tubercle bacilli than many other concentration methods.] In 43, or 11·2%, of the 385 specimens examined, some growth occurred on the drug-containing media, 39 of these specimens being from the fresh cases and 4 from the reactivated cases. The growth of the organisms in these 43 cases in the presence of the drugs, separately and combined and in various concentrations, was compared with the growth on the drug-free medium, and it was concluded that in 6 (1·6%) of the 385 sputum-positive cases of untreated disease the organism was significantly resistant to streptomycin and in 9 (2·3%) it was significantly resistant to isoniazid. In no case was there any significant resistance to a combination of both drugs. *John M. Talbot*

626. **Infection with Drug-resistant Tubercle Bacilli**
F. BECK. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 151–157, Aug., 1955. 5 refs.

Out of approximately 600 cases of recent tuberculous infection of the lungs admitted to the Ray Brook State Tuberculosis Hospital, Ray Brook, New York, tubercle bacilli were recovered from about 80%. In 10 cases, or approximately 2% of those with positive sputum, the infecting organism was found to be resistant to streptomycin, 2 strains being also resistant to PAS. Infection was from a known source in 8 cases, and in 6 of them was undoubtedly acquired in a hospital. It is not considered, therefore, that infection with drug-resistant mycobacteria represents at the moment a serious public health problem. *John M. Talbot*

627. **Are Chemotherapy and Collapse Therapy for Pulmonary Tuberculosis Compatible? I. A Study in Cavities in the Lower Lobe**
T. KUMAGAI, C. SUZUKI, S. OKA, T. KUROBANE, I. KANNO, S. SATO, S. AWATAGUCHI, Y. NIITU, and H. UEDA. *Reports of the Research Institute for Tuberculosis and Leprosy, Tohoku University* [*Rep. res. Inst. Tuberc. Lepr. Tohoku Univ.*] **6**, 133–188, March, 1955 [received Sept., 1955]. 57 figs., 11 refs.

The authors of this paper from Tohoku University, Sendai, Japan, begin by drawing attention to the contradictory opinions prevailing on the treatment and prognosis of tuberculous cavitation of the lower lobes of the lungs. In an attempt to shed some light on this problem they studied 111 patients divided into 2 classes: (A) 41 patients with cavitation of the basal segments; and (B) 70 patients with cavitation of the apical segment of the lower lobe. Each class was then divided into 3 groups: (1) 9 and 16 patients respectively who were treated by chemotherapy alone; (2) 12 and 27 patients respectively treated by collapse therapy alone; and (3) 20 and 27 patients respectively treated by combined collapse therapy and chemotherapy.

In Class A it was found that cavity closure was effectively brought about by either chemotherapy or collapse therapy, the former being the superior method. Much to the authors' surprise, however, the combined treatment produced the poorest results, for in two-thirds of the cases the cavity failed to close and most of the patients remained sputum-positive. In Class B practically the same results were obtained, except that the outcome in Group 3 was not quite so bad as in Class A. These findings are difficult to explain, but the authors suggest that it may be found in the different manner of healing produced by chemotherapy and collapse therapy. The former brings about expulsion of the contents of the cavity through a patent bronchus followed then by absorption and epithelization. Collapse therapy tends to cause kinking and obliteration of the bronchial lumen, which may well frustrate the effect of chemotherapy.

[This is a long article and is taken up mostly by case-histories and reproductions of radiographs. The authors' conclusions are, to say the least, somewhat surprising, and probably few phthisiologists in Great Britain would agree with them.] *Paul B. Woolley*

628. **A Comparison of the Results of Thoracoplasty and Pulmonary Resection**
C. SUZUKI, H. MIZUNO, and H. NAKAYAMA. *Reports of the Research Institute for Tuberculosis and Leprosy, Tohoku University* [*Rep. res. Inst. Tuberc. Lepr. Tohoku Univ.*] **6**, 189–206, March, 1955 [received Sept., 1955]. 2 refs.

In view of the difficulty frequently experienced in deciding between thoracoplasty and resection for the treatment of cases of pulmonary tuberculosis the authors have compared the results obtained at Tohoku University Hospital, Sendai, Japan, from these two operations between April, 1950, and March, 1953, with special reference to mortality, postoperative complications, sputum conversion, and postoperative state. Of 357 patients treated, 227 underwent thoracoplasty (Group 1) and 130 resection (Group 2). The duration of the disease was less than 3 years in 31·2% of cases in Group 1, whereas the corresponding figure in Group 2 was 80%. In each group more than 50% of the patients had far-advanced disease. There were cavities in 88·5% of cases in Group 1 and in 65·4% in Group 2; the sputum was positive for tubercle bacilli in 92·9% and 80% respectively. Endobronchial disease was present in 43·2% of the 219 patients in Group 1 who were subjected to bronchoscopy and in 49·2% of the 111 in Group 2. Pre- and post-operative chemotherapy covered a period of a few weeks only in both groups. Thoracoplasty was performed under local analgesia in all cases, whereas resection was performed under local analgesia " at the early stage " [? of the disease] and later under general anaesthesia; upper lobectomy or pneumonectomy was followed by modified thoracoplasty.

The mortality within 2 months of operation was 0·9% in Group 1 and 3% in Group 2, and between 2 months and 4¼ years after operation the figures were 1·3% and *nil* respectively. Thus the over-all mortality was roughly equal in the two groups. Ipsilateral or contralateral spread occurred in 6·5% of cases in Group 1 and in 11·4% in Group 2. Resection was complicated by bronchial fistula and empyema in 2·2%, ulceration of

the bronchial stump in 10%, and atelectasis in 9·2% of cases. Of the 222 patients who survived thoracoplasty, 119 (53·6%) became fully active; among the 126 survivors of resection the corresponding figure was 60 (46·1%).

The authors consider that thoracoplasty is to be preferred for patients who have bilateral disease and that this operation is also probably the safest procedure for old patients with long-standing disease. Their over-all impression, however, is that the final result is dependent, in the main, on factors other than choice of operation.

Paul B. Woolley

* See also Pathology, Abstract 587.

EXTRA-RESPIRATORY TUBERCULOSIS

629. **The Treatment of Tuberculosis of the Urinary Tract in Children.** (Zur Therapie der Tuberkulose der ableitenden Harnwege im Kindesalter)
H. KLEINBAUM. *Tuberkulosearzt* [*Tuberkulosearzt*] **9**, 483–493, Aug., 1955. 3 figs., 32 refs.

Writing from the Children's Clinic of the University of Kiel, the author describes a series of 11 cases of tuberculosis of the urinary tract in children aged 4 to 16 years, all of which were treated conservatively. In 10 cases there was an associated renal lesion, while in one case the infection of the ureter was assumed to have arisen from a partially calcified mesenteric lymph node by direct spread. Four patients also suffered from pulmonary tuberculosis, while 7 had lesions of bone, including tuberculous spondylitis in 5 cases. In all 11 cases the presenting symptoms were sterile pyuria with frequency and dysuria. Cystoscopy, which was carried out at this stage in 5 cases, revealed the characteristic picture of mucosal thickening and erythema at the ureteric orifice with a few subepithelial nodules. In one case ulceration of the mucosa had produced an attack of renal colic, the same symptoms being produced in another case by a stone, formed as a sequela of the tuberculous infection. In 2 cases tuberculous ulcers of the bladder mucosa were already present when the patient was first seen, while in 3 cases the disease had penetrated to the muscular coat and produced considerable reduction in bladder volume. Bacteriological proof was obtained in all cases by culture and guinea-pig inoculation between 3 weeks and 5 months after the appearance of symptoms.

Various treatment schedules were employed, but the principle of prolonged chemotherapy was maintained throughout the series. In 5 cases thiacetazone, 1 to 2 mg. per kg. body weight, was given daily together with 40 mg. of streptomycin per kg. (up to a maximum dose of 1 g.) every third day for 10-day periods, alternating with 5-day courses of PAS, 6 g. daily for children up to 6 years of age and 12 to 16 g. for older children. This regimen was maintained for 6 months in 4 cases, and for a year in one. The author gives a warning against the toxic effect of thiacetazone on small children, nausea, vomiting, and listlessness being indications for its immediate withdrawal. He considers it to be contraindicated in cases with involvement of bone, and treated 3 such cases in the present series by a regimen similar to the one outlined above, but substituting isoniazid, 10 mg. per kg., for thiacetazone. A further 4 cases were treated by the continuous administration of streptomycin and PAS for a period of 6 months.

The results were good in all 11 cases, the clinical condition and cystoscopic appearances improving, pyuria clearing up, and the urine becoming sterile. During a follow-up period of unspecified length none of the patients developed symptoms of recurrence, but one had a residual hydro-ureter and one a residual hydronephrosis, while one later required nephrectomy for an unspecified residual condition.

In 4 of the cases of tuberculous cystitis instillations of 5 ml. of a 10% solution of " solvoteben " were given on alternate days for 3 weeks. The treatment was well tolerated and appeared to exert a favourable influence on the healing of the ulcers. *H. F. Reichenfeld*

630. **Tuberculous Meningitis: the Diagnostic and Prognostic Significance of Spinal Fluid Sugar and Chloride**
H. W. GIERSON and J. I. MARX. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 902–908, April, 1955. 8 refs.

The concentrations of sugar and chloride present in the cerebrospinal fluid (C.S.F.) before treatment in 231 cases of tuberculous meningitis admitted to the Los Angeles County Hospital between 1947 and 1953 are analysed in this paper to determine their diagnostic and prognostic significance. The normal values adopted were 50 to 80 mg. per 100 ml. for sugar and 120 to 130 mEq. per litre for chloride. Of the 161 cases in which the levels were determined in the initial specimen of C.S.F. taken on admission, both values were diminished in 68%, the sugar content only in 7·5%, and the chloride content only in 17%, while in 7·5% both values were normal. But after the first few days in hospital and before starting treatment the corresponding figures were 72·7, 5·6, 20, and 1·7% (of all 231 cases) respectively. The authors therefore conclude that the chloride content provides a more reliable diagnostic index than the sugar content. When both sugar and chloride levels remained normal the prognosis was apparently better than when either was depressed, while the survival rate was poorest when both values were below normal. (The over-all survival rate in the series was only 39·5%). For prognostic purposes the chloride level was again considered more reliable than the sugar level, although neither was a particularly accurate or sensitive index. These findings are acknowledged to be at variance with those of other observers.

[It is justifiable to draw conclusions from an investigation such as this only if the analysis is confined to data from cases in which the diagnosis has been established without doubt, preferably by the isolation of tubercle bacilli from the C.S.F. No mention is made of the isolation of tubercle bacilli or of any other diagnostic criteria used. The figures and conclusions must therefore be accepted with reserve.] *John Lorber*

Venereal Diseases

631. **Studies on the Treponemal Immobilization Test. III. Use of the TPI as a Verification Test in Suspected Latent Syphilis**
A. E. WILKINSON and P. J. L. SEQUEIRA. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 143–154, Sept., 1955. 47 refs.

The authors have investigated, at the Venereal Diseases Reference Laboratory (London Hospital), London, the value of the treponemal immobilization (T.P.I.) test in confirming a diagnosis of suspected latent syphilis and in the examination of "problem" sera. They showed that immobilizing antibody was demonstrable in all but one of 136 patients in whom the diagnosis of latent syphilis was corroborated by evidence other than that of the results of serum tests for syphilis alone. The T.P.I. reaction was negative in 11·5% of 200 untreated patients coming to venereal disease clinics with suspected latent syphilis, and in 4·4% of 248 such patients who had been diagnosed and treated for latent syphilis in the past.

On examination of problem sera from 69 subjects volunteering as blood donors and from 244 pregnant patients 35% of the former and 27·5% of the latter gave a negative result in the T.P.I. test, although all of them had given a positive result in standard serum tests for syphilis on routine testing. In an unselected group of antenatal sera about one-fifth of those positive to the standard serum tests for syphilis were T.P.I.-negative. Of 149 patients with diseases other than syphilis in whom there had been a positive reaction to standard serum tests for syphilis on routine testing, 29% gave a negative reaction to the T.P.I. test.

The results of the T.P.I. test were then compared with those of four standard serum tests for syphilis on sera from 572 untreated patients. This comparison showed disagreement with the standard Wassermann reaction in 13%, with the Wassermann reaction with cardiolipin in 23%, with the Kahn reaction in 17%, and with the P.P.R. (Price precipitation reaction) in 10%. It is concluded that in view of its specificity and great sensitivity the T.P.I. test is eminently suitable as a verification test in cases of suspected latent syphilis. *R. R. Willcox*

632. **A Serological Survey for the Detection of Syphilis in 21,437 Recruits.** (Enquête sérologique en vue du dépistage de la syphilis chez 21,437 recrues)
—. DUTREY, —. OLIVIER, —. BÉNAZET, and —. REBOUL. *Presse médicale* [*Presse méd.*] **63**, 1027–1028, July 9, 1955. 1 ref.

Routine serological tests for syphilis were carried out on 21,437 recruits called up for military service with the French army during the period 1952–4. The majority were 20 years old, but the series included a small number of men aged 23 to 25. The recruits came from both rural and urban areas and represented all social classes in Metropolitan France. The Kline exclusion test or the Meinicke micro-reaction were used as screening tests, and all reactive sera were then subjected to the standard Kahn and Kline tests and the Debains and Kolmer complement-fixation tests. Men whose serum gave a positive reaction with one or more of the standard tests were investigated clinically and a treponemal immobilization (T.P.I.) test was carried out on a further specimen of serum.

The screening test gave positive reactions in 124 cases (0·57%), but positive reactions with one or more of the standard tests were obtained with only 32 of these sera. Of these 32 sera, 12 gave a positive and one a doubtful reaction to the T.P.I. test. Thus on the basis of the results of the T.P.I. test the incidence of syphilis revealed by the survey was 0·06% (13 cases). Of these 13 patients, one had secondary lesions (the T.P.I. reaction being doubtful in this case), 4 had a history suggestive of recent early lesions, 2 had latent congenital syphilis, and 6 had no clinical evidence or history of syphilis.

The very low incidence of syphilis noted is attributed to the men's average age, to their having been born at a time when measures against syphilis were becoming effective (thus reducing the incidence of congenital infection), and to the probable rejection for service of men with overt congenital lesions. In contrast, a similar survey of a small number (346) of North African recruits showed the incidence of syphilis among them to be much higher (4·9%).

Of those cases in which all four of the standard tests gave a positive result, the T.P.I. reaction was positive in all but one, and in this case a positive result was obtained on examination of a second specimen of serum. On the other hand, of the 22 cases in which the results of the standard tests were only weakly positive or dissociated, only 3 gave a positive T.P.I. reaction. A possible cause for non-specific serum reactions was found in only one case, in which the patient was found to have virus pneumonia. *A. E. Wilkinson*

633. **Cardiolipin Antigen. VIII. Course of and Mutual Relations between Various Seroreactions in Syphilis-infected Rabbits.** [In English]
H. SCHMIDT. *Acta pathologica et microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **37**, 252–266, 1955. 6 figs., 31 refs.

634. **The Decline and Fall of Syphilis in New York State. III. Early Acquired Syphilis**
R. L. VOUGHT, L. DE MELLO, and F. B. LOCKE. *Journal of Chronic Diseases* [*J. chron. Dis.*] **2**, 303–310, Sept., 1955. 3 figs., 3 refs.

See also Microbiology and Parasitology, Abstracts 601–2.

Tropical Medicine

635. **Kwashiorkor and Protein Malnutrition. A Dietary Therapeutic Trial**
J. F. Brock, J. D. L. Hansen, E. E. Howe, P. J. Pretorius, J. G. A. Davel, and R. G. Hendrickse. *Lancet* [*Lancet*] **2**, 355–360, Aug. 20, 1955. 2 figs., 16 refs.

As part of a comprehensive investigation into kwashiorkor and protein malnutrition an attempt was made to determine the nutrients in skimmed milk which are responsible for " initiating cure " of the disease—that is, for the definite reversal of direction of progress which is evident after 3 weeks' diet of skimmed milk. The patients, most of whom were under 2 years of age, were treated in hospitals in Pretoria (77 patients), Durban (40), and Cape Town (18). The investigation was carefully controlled statistically. Cases in which additional treatment, such as antibiotics or blood transfusions, was necessary were regarded as failures. The nutrients tested were: (1) dried skimmed milk; (2) dried skimmed milk with supplements of vitamin A, vitamin-B complex, ascorbic acid, and calciferol; (3) vitamin-free casein with glucose and a mineral mixture; and (4) vitamin-free casein with mineral and vitamin mixtures. It was found that nutrient (1) was sufficient alone to initiate cure, with improvement in the serum protein level, and that the results obtained with (2), (3), and (4) were not significantly different from those obtained with (1). Since nutrients (3) and (4) did not contain albumin, globulin, or fat, and the vitamin and glucose supplements were without effect, it is suggested that the casein, mineral fraction, or trace-element fraction, or all three, contained the curative factor. Further trials are in progress to identify this factor.

In an addendum, 9 cases are briefly discussed in which the same degree of success was obtained with a mixture containing 18 amino-acids with minerals and vitamins.

H. E. Magee

636. **Acute Toxic Hypoglycaemia Occurring in the Vomiting Sickness of Jamaica. (Clinical Aspects)**
K. L. Stuart, D. B. Jelliffe, and K. R. Hill. *Journal of Tropical Pediatrics* [*J. trop. Pediat.*] **1**, 69–87, Sept., 1955. 6 figs., 20 refs.

The " vomiting sickness " has been known as a disease entity in Jamaica for many years. Scott, in 1916, was one of the first to give a detailed description of the disease, including its morbid anatomy, and this paper from the University College of the West Indies brings the clinical picture up to date.

The disease generally occurs in poorly nourished Jamaican peasants, and mainly affects children. It has an abrupt onset, with vomiting and collapse, but rarely with diarrhoea. Mortality is high, death occurring in coma, sometimes within a few hours of onset. Fulminating cases in which there is no vomiting also occur, the patient becoming rapidly comatose. The aetiology is as yet unknown, but the disease is generally attributed to the effects of a toxin of some sort. Scott was of the opinion that all cases were due to the eating of the unripe ackee—the fruit of *Blighia sapida*, which is widely grown and eaten on the island, and which has been shown to contain a toxic saponin when immature. However, cases have been reported in persons who had not eaten ackees. The disease is usually associated with malnutrition, but it is unknown in areas outside Jamaica where similar or worse degrees of poverty exist. Its abrupt and often explosive onset suggests the action of some specific toxin, while the fact that where whole families are affected infants fed entirely on milk escape seems to indicate some article of diet as the source.

Details are given of 2 cases of vomiting sickness in adults and 9 in children. Both the adults recovered, but 3 of the children died in hospital and one was dead on admission. The main features were sudden onset, with vomiting, changes in the mental state (with coma or convulsions in severe cases), and hypoglycaemia, which may reach an extreme degree and fails to respond to adrenaline. In one 3-year-old child the blood sugar level fell to 3 mg. per 100 ml. Biopsy of the liver was performed in most cases, marked glycogen depletion being found. The treatment given included administration of glucose (either intravenously or by mouth) and fluids to combat hypoglycaemia and dehydration, and sedation. In addition, the authors suggest the use of aneurin, nicotinic acid, and also possibly ACTH (corticotrophin). As a preventive measure the eating of unripe ackees has been discouraged in public health propaganda in the island for some years. The mechanism of the hypoglycaemia is discussed and the hypothesis put forward that it is due to a temporary blockage caused by an unknown toxin in the enzyme systems responsible for gluconeogenesis. [But this postulates that the toxin has a selective action on certain Jamaican people, mostly children, which seems unlikely.]

W. K. Dunscombe

637. **The Hepatic Glycogen Content in Acute Toxic Hypoglycaemia**
S. J. Patrick, D. B. Jelliffe, and K. L. Stuart. *Journal of Tropical Pediatrics* [*J. trop. Pediat.*] **1**, 88–89, Sept., 1955. 3 refs.

Details are given of a micro-method used for the estimation of the glycogen content of biopsy specimens of liver tissue in cases of Jamaican " vomiting sickness ". [See Abstract 636. For details of the technique the original paper should be consulted.] Comparison of the results obtained by macro- and by micro-methods of hepatic glycogen estimation in rats revealed good agreement.

The findings in 4 cases of the disease in which the blood sugar level and hepatic glycogen content were determined are recorded. There was a considerable reduction in the blood sugar content, which ranged from 15 to 21 mg. per 100 ml., and a relatively enormous diminution in

the liver glycogen content, the normal value for which is 5 to 10% of the wet weight, whereas in 4 cases investigated the lowest values were less than 0·2% and the highest only 0·7%. During the acute stage there was a complete lack of response of the blood sugar level to the subcutaneous injection of adrenaline. Liver biopsy taken after recovery in one of these cases showed the liver glycogen content to have returned within normal limits (7·5%), having been less than 0·2% in the acute stage. *W. K. Dunscombe*

638. **Acute Toxic Hypoglycaemia Occurring in the Vomiting Sickness of Jamaica. Morbid Anatomical Aspects**

K. R. HILL, G. BRAS, and K. P. CLEARKIN. *West Indian Medical Journal* [*W. Indian med. J.*] **4**, 91–104, June, 1955 [received Sept., 1955]. 5 figs., bibliography.

This paper from the University College of the West Indies deals particularly with the morbid anatomy and histology of Jamaican " vomiting sickness " [see Abstract 636]. The laboratory and post-mortem findings in 7 cases in children are reported, together with the clinical and laboratory findings in one case in an adult, who recovered. The children's ages ranged from just under 2 years to 6¼ years.

The significant findings at necropsy included alimentary lymphoid hyperplasia—in one case it is recorded that " the mesenteric lymph nodes were swollen up to 10 cm. in diameter "—tissue oedema, extensive fatty metamorphosis of the liver and kidneys, and pre- and post-mortem hypoglycaemia with complete absence of glycogen from the liver cells in those cases in which glucose infusions were not given before death. The authors state that there was no morphological evidence that the endocrine glands play any significant part in causing the hypoglycaemia [although haemorrhages were found in the adrenal glands in 3 cases out of 7]. Despite the clinical impression in Jamaica that vomiting sickness occurs predominantly in the lowest economic classes and consequently that malnutrition probably plays a part, in only one of the cases reported in children was the nutritional state recorded as " poor ".

[Since the paper contains a number of obvious misprints, the remarkable figure quoted above for the size of the mesenteric lymph nodes—if it refers to the individual nodes—needs to be confirmed. The paper as a whole and the photomicrographs illustrating it are good.] *W. K. Dunscombe*

639. **Clinical Observations on Veno-occlusive Disease of the Liver in Jamaican Adults**

K. L. STUART and G. BRAS. *British Medical Journal* [*Brit. med. J.*] **2**, 348–352, Aug. 6, 1955. 5 figs., 11 refs.

The authors describe from the University College of the West Indies the condition of veno-occlusive disease of the liver, a term given on histological grounds to a form of liver disease occurring frequently in Jamaican children and occasionally in adults. The disorder falls roughly into three stages, acute, subacute, and chronic, but these are often ill-defined. In the acute stage in children there is sudden onset of abdominal pain, hepatomegaly, and ascites, which may subside in 7 to 14 days. The majority of patients at this stage recover completely, but in some the disease passes into the subacute stage, which may be asymptomatic except for occasional exacerbations. In the chronic stage cholaemia and cirrhosis develop more rapidly than in cirrhosis due to other causes. Death may result from hepatic failure or ruptured oesophageal varices.

Biopsy and post-mortem examination of the liver show that the basic hepatic lesion is an acute congestion due to blocking of the smaller hepatic veins by subintimal thickening which causes obstruction to the outflow of portal blood. The authors suggest this may possibly be a result of protein deficiency, which would also explain the ascites, since it has been shown that protein depletion affects capillary permeability; they therefore relate the condition to common deficiency cirrhoses. Moreover, a high-protein diet is the best treatment, although not a specific cure. Liver function tests show moderate impairment of hepatic function at the onset, but the serum albumin and cholinesterase levels are the best prognostic guides. A comparison is drawn between the rapid appearance and disappearance of ascites and the high protein content of the ascitic fluid in this condition and in the experimental ascites produced by ligation of the thoracic vena cava in the dog. *Clement C. Chesterman*

INFECTIOUS DISEASES

640. **A Preliminary Trial of the Use of Banocide as a Prophylactic against Filarial Fever**

L. NEVILL. *East African Medical Journal* [*E. Afr. med. J.*] **32**, 337–340, Aug., 1955. 1 fig.

A simple [and admittedly inconclusive] investigation was carried out in the Tana River district of Kenya to determine whether it was possible to banish microfilariae of *Wuchereria bancrofti* from the blood by small prophylactic doses of " banocide " (diethylcarbamazine) without the risks attaching to heavy dosage needed for mass treatment. A single riverine village with a population of about 300 was chosen for the purpose of this investigation. At the start specimens of night blood from 281 of the inhabitants were examined, and of these 12 were found to be positive for *W. bancrofti*. In addition there were 10 cases of elephantiasis in the community. Banocide was given in tablet form, 123 adults receiving 1 or 2 tablets daily for 6 weeks and 80 children receiving half the adult dose [the amount in each tablet is not stated]. For control purposes 51 adults and 57 children received tablets of calcium. Absence of filarial fever [a rather indeterminate entity] was the criterion of efficacy of the drug. During the 6-week period of the trial 14 cases of filarial fever occurred—6 in the first week and the remainder before the end of the third week. No further cases were observed, and at the end of the investigation all the blood specimens examined (231) were negative.

[There was no long follow-up in this investigation. If it be assumed that each tablet contained 50 mg. of

the drug, it seems unlikely that a dose of 1 to 2 mg. per kg. body weight would have remained effective for long, since as much as 25 mg. has failed to achieve a cure. In order to assess the value of the trial, additional evidence from the larval index of the mosquitoes, *Taeniorhynchus* (*Mansonia*) *africanus* and *T. uniformis*, before and after would be necessary.] *Clement C. Chesterman*

641. Lesions of the Intrahepatic Portal Radicles in Manson's Schistosomiasis

F. LICHTENBERG. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 757–771, July–Aug., 1955. 15 figs., 22 refs.

The report here presented from the University School of Tropical Medicine, San Juan, Puerto Rico, is based on 27 necropsies and 4 biopsy specimens of liver tissue in 31 cases of Manson's schistosomiasis. Three types of lesion of the intrahepatic portal radicles are described. (1) The most common was replacement of the radicles by granuloma, which was found to occur independently of hepatic fibrosis. The portal venous lumen was still discernible and contained an egg of *Schistosoma mansoni*, sometimes fragmented and frequently engulfed by a multinucleated cell. The endothelium was swollen and proliferated, and the media degenerated and invaded by leucocytes, eosinophils, epithelioid cells, and macrophages. (2) Sclerosis and narrowing. In most cases this lesion was accompanied by fibrosis, the lumen of the portal vein being greatly narrowed or subdivided owing to invasion by fibrous tissue which was continuous with that outside the vessel; there was little inflammation. In some cases ova and granulomata were present. (3) The rarest and most severe lesion was intrahepatic thrombophlebitis which in one case affected up to nearly one-half of the radicles in the liver; larger veins were also affected. The portal vein was only slightly smaller than normal, but its lumen was entirely filled with fibrous and inflammatory tissue through which sometimes passed tortuous vascular channels, the media being atrophied and almost destroyed. Numerous ova, occasionally surrounded by pseudotubercles, were present. The surrounding fibrous tissue also frequently contained ova and pseudotubercles.

The lesions seen appeared to be sufficiently great to cause portal hypertension; they resembled the lesions seen elsewhere, notably in the lung, and appear to have a similar pathogenesis. *W. H. Horner Andrews*

642. Thiosemicarbazone as an Additive in the Treatment of Leprosy

A. R. DAVISON. *International Journal of Leprosy* [*Int. J. Leprosy*] **23**, 19–22, Jan.–March, 1955 [received Sept., 1955].

At Westfort Institution, Pretoria, 43 patients (13 Europeans and 30 Bantus) with leprosy were treated with thiacetazone (thiosemicarbazone) and the results after 3½ years are here reported. The tuberculoid type of the disease was present in 6 cases and lepromatous leprosy in the remainder. The drug was given in a dosage of 25 mg. daily for the first week, rising to a maximum of 200 mg. daily in the fifth week. The patients were disappointed with the initial results, and in most cases the treatment had to be supplemented after 6 months with sulphones or isoniazid. The period of observation of the effects of thiacetazone alone was rather short, but the author was able to study its effects in combination with isoniazid or sulphones. In the tuberculoid form of the disease the results were satisfactory, but improvement was slower than with sulphone therapy only. In the lepromatous cases clinical improvement was noted in some cases within 3 months and in most of them within a year. Laryngeal ulceration healed in all the 3 cases in which this was present. The bacterial content of the lesions was reduced, but at the end of the 3½ years the bacteriological findings were negative in only 4 cases, in 3 of which sulphones had been given for as long as 6 years. Albuminuria was observed during treatment in nearly all the cases, and transient jaundice in 2. The author concludes that thiacetazone is of some value in the treatment of tuberculoid leprosy, but that it is of doubtful value alone in lepromatous leprosy and does not enhance the therapeutic effect of the sulphones. *William Hughes*

643. Clinical and Therapeutic Study of an Antigen Prepared with *Mycobacterium marianum*, Applied to 457 Leprosy Patients

M. BLANC, M. PROST, —. MICHEAL, —. LEMAIRE, E. KUNA, J. ESSELE, and J. M. NKOA. *International Journal of Leprosy* [*Int. J. Leprosy*] **23**, 23–31, Jan.–March, 1955 [received Sept., 1955]. 4 refs.

At Nden Leprosarium, French Cameroons, an antigen prepared from *Mycobacterium marianum* was tried in the treatment of leprosy. Reference is made in the text to previous papers in which the preparation of the antigen from the " Chauviré " strain of the organism is described. Over a recent 2-year period 1,000 patients were treated and in the present paper the results obtained in 457 of these are analysed. The antigen was injected intradermally into the left arm once a month for 3 months; after a rest period of 2 months three further injections were given at monthly intervals. More recently six consecutive injections were given without a rest period. Reactions of varying intensity were observed. In mild cases there was itching at the site of the injection, followed on the third day by the development of a papule. In severe cases the reaction was reminiscent of the Koch phenomenon. The local reaction proceeded to necrosis and ulceration at the site of injection. The focal reaction involved the regional lymph nodes and the leprotic lesions, in which haemorrhage was sometimes seen. The general reactions included fever, temperature in some cases exceeding 39° C. and persisting for 8 to 10 days, headache, and generalized pruritus. The reactions were weak or moderate in 82% of the patients and severe in the remainder. During a period of observation of more than 2 years 10 patients died, but in no case was death attributable to the injections. In 27% of all cases observed for 6 months or longer the condition was unchanged or worse; in the remainder there was improvement, this being marked in 20%. These results are considered to be as good as those obtained with sulphone therapy. *William Hughes*

644. Infantile Visceral Leishmaniasis in the Maltese Islands

T. J. AGIUS-FERRANTE. *British Medical Journal* [*Brit. med. J.*] **2**, 654–656, Sept. 10, 1955. 15 refs.

The purpose of this paper is to draw attention to the decline in the incidence of leishmaniasis in the Maltese islands, where the disease has been endemic since the early years of the present century. The cutaneous form of the disease is unknown in Malta, although it is encountered in Italy. The total number of cases of the visceral type, which mainly affects children between 1 and 3 years of age, seen in Malta from 1947 to 1954 inclusive was 777 (386 males and 391 females). During this period there were 29 deaths, 21 of which occurred in the years 1947 and 1948. Since the end of 1946 disinfestation with D.D.T. has been carried out on all premises where cases of leishmaniasis have been notified. The sudden fall in the number of cases—from 191 in 1947 and 204 in 1948 to 91 in 1949—and the continuing fall—63 cases in 1953 and 49 cases in 1954—appear to be due to residual spraying with D.D.T. The sandfly is considered to be the vector, and all rooms in infected premises are sprayed twice, with an interval of one month between the first and second spraying. This procedure has been so successful that leishmaniasis is no longer a serious problem in Malta, and may even become a "very rare condition". *R. R. Willcox*

645. Potentiation of the Curative Action of Primaquine in Vivax Malaria by Quinine and Chloroquine

A. S. ALVING, J. ARNOLD, R. S. HOCKWALD, C. B. CLAYMAN, R. J. DERN, E. BEUTLER, and C. L. FLANAGAN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 301–306, Aug., 1955. 21 refs.

At the U.S. Army Malaria Research Unit, University of Chicago, three groups, each of 19 volunteers from a State penitentiary without history of exposure to malaria, were infected with the Chesson strain of *Plasmodium vivax* by mosquito bite, the same 10 mosquitoes being used in rotation to infect groups of 3 men, one from each experimental group. Parasitaemia and fever appeared in all volunteers by the 14th day after infection.

Treatment was begun immediately the patients developed a temperature of 102° F. (38·9° C.) and parasites had been demonstrated in the blood on 2 consecutive days, the following drug regimens being employed. Group 1 received quinine (2 g. of quinine sulphate divided in 6 doses daily for 14 days) followed after an interval of 2 days, to allow of the excretion of quinine, by primaquine in doses of 15 mg. (base), also divided in 6 doses daily, for a further 14 days. Group 2 received quinine and primaquine in the same dosage as before, but concurrently. Group 3 received chloroquine concurrently with primaquine, the dose of the latter being as before, together with 0·6 g. of chloroquine on the first day followed in 24 hours by 0·4 g., a total dose of 1 g. having been shown to be suppressive.

As a result of this treatment there were 15 relapses in Group 1, only one relapse in Group 2, and 5 in Group 3, all relapses occurring after expiration of the limit of 30 days covering possible recrudescence of the Chesson strain. The results demonstrate the apparent potentiation of the action of primaquine by the concurrent administration of either quinine or chloroquine.

B. G. Maegraith

646. Compatibility of Sickling with Malaria

G. A. DELIYANNIS and N. TAVLARAKIS. *British Medical Journal* [*Brit. med. J.*] **2**, 301–302, July 30, 1955. 10 refs.

It has been suggested that the survival at high frequency of the potentially lethal gene which is responsible for the sickling phenomenon may be the result of some special advantage conferred by it, such as a high resistance to malaria. The authors had the opportunity of investigating this hypothesis in Chaldiki, where malaria is endemic and the incidence of sickling is high.

In 136 out of 174 cases of malaria reported to the Department of Malaria in Northern Greece during the three-year period 1952–4 they examined the patient's blood for sickling. Although these patients all came from villages with high rates of sickling (18 to 32%), the mean rate of sickling amongst them was only 5·8%.

Moreover, investigation of the blood of siblings of children infected with malaria showed that the malaria parasite was usually absent when the sickling phenomenon was present, whereas the blood of many of the non-sicklers was infected. It is concluded that individuals with the sickle-cell phenomenon and trait are more resistant to malaria than normal individuals in this area.

H. Lehmann

647. Tetracycline in the Treatment of Intestinal Amebiasis

H. SENECA. *Antibiotic Medicine* [*Antibiot. Med.*] **1**, 221–224, April, 1955. 29 refs.

After a rapid but concentrated review of the use by previous workers of antibiotics in the treatment of amoebiasis the author reports, from Columbia University College of Physicians and Surgeons, New York, that 19 out of 20 cases of chronic intestinal amoebiasis were successfully treated with "tetracyn" (tetracycline). The patients were 5 females and 15 males aged from 26 to 55 years, and the duration of the infection ranged from 18 months to more than 10 years. In 3 cases trophozoites were present in the stools, and in the others cysts. *Streptococcus faecalis* was isolated from 5 patients, but no *Shigella* or *Salmonella* organisms were found in any of the cases.

The tetracycline was given in a dose of two 250-mg. tablets 3 times daily for 8 days, to a total dose of 12 g. The stools were examined at the end of one and 3 months following treatment; some of the patients were observed for about 9 months and a few for only 6 weeks. The amoebae disappeared from the stools in all 19 cases and the patients' physical condition improved. In most cases a diet high in protein, carbohydrate, and vitamins was also given. The antibiotic was well tolerated by all the patients but one, in whom it had to be discontinued. In 7 cases a second course of tetracycline was given.

[No details of the cases are given; it should be recalled that other antibiotics have been used in the treatment of intestinal amoebiasis with varying degrees of success.]

R. Wien

Allergy

648. Studies in Sensitization as Applied to Skin Test Reactions. III. Influence of Age upon Skin Reactivity
L. TUFT, V. M. HECK, and D. C. GREGORY. *Journal of Allergy* [*J. Allergy*] **26**, 359–366, July, 1955. 3 figs., 2 refs.

In this study reported from Temple University Hospital, Philadelphia, 100 patients in each decade of life from 0 to 70+ were skin-tested for allergy to a wide range of foodstuffs. It was found that the percentage of positive reactions decreased sharply with age, irrespective of whether the foods tested were those commonly or rarely eaten. In a further study skin tests with varying concentrations of histamine ranging from 1 in 1,000 to 1 in 100,000 were carried out on 100 normal subjects in each decade of life. Here also the skin sensitivity declined sharply from decade to decade for all histamine concentrations, a markedly positive reaction to a concentration of histamine of 1 in 1,000 being obtained in 75% of subjects in the first decade and only in 12% of those in the 8th decade. It is concluded that the failure to obtain a positive skin reaction in older persons may be due rather to a loss of skin reactivity than to a lack of specific sensitivity. *H. Herxheimer*

649. The Provocation of Dyspnoea with Acetylcholine as a Diagnostic Test for Respiratory Allergy. (Test de la dyspnée provoquée par l'acétylcholine et diagnostic de l'allergie respiratoire)
R. PANZANI. *International Archives of Allergy and Applied Immunology* [*Int. Arch. Allergy*] 7, 25–41, 1955. 1 fig., bibliography.

The author claims that observation of the degree of dyspnoea produced by acetylcholine offers a useful contribution to the diagnosis of minor and atypical forms of respiratory allergy. Spirometric recordings were obtained after forced expiration, before and after inhalation of a 1% acetylcholine aerosol administered for 1 to 3 minutes. No alteration in vital capacity was observed in normal subjects or in non-allergic individuals suffering from infective conditions of the respiratory tract. On the other hand the values for vital capacity, total pulmonary capacity, and especially maximum available volume were all demonstrably reduced in patients with allergic conditions of the respiratory tract, neurodermatitis, and emphysema. *Kate Maunsell*

650. Special Features in Allergy in Children. [In English]
Z. ERIKSSON-LIHR. *Acta allergologica* [*Acta allerg. (Kbh.)*] 8, 289–313, 1955. 11 figs., 37 refs.

The author reviews and analyses in considerable detail the incidence of allergic diseases in childhood in Finland, the findings being based in part on the school medical records of nearly 30,000 children between the ages of 7 and 14 in Helsinki and partly on those of a smaller series of 4,382 schoolchildren in Türkü. Data for the incidence and severity of the various types of allergic disease were derived from the records of 4,059 patients who attended or were admitted to the Hospital for Allergic Diseases, Helsinki, during the period 1951–4.

The over-all incidence of allergic diseases in Türkü was 6·8% and in Helsinki 3·6%. The incidence of the different allergic manifestations are tabulated. The incidence of asthma was higher in boys and that of eczema higher in girls. In general, allergic symptoms developed earlier in the former, infection appearing to be more important aetiologically in girls, while the allergic factor was more important in boys. The author produces evidence to show that the allergic diseases are due to a relative insufficiency of the pituitary–adrenocortical system and that the function of the adrenal cortex in boys is inferior to that of girls. *A. W. Frankland*

651. Treatment of Bronchial Asthma with Corticotrophin (ACTH). (Лечение бронхиальной астмы адренокортикотропным гормоном (АКТГ))
B. B. KOGAN. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 49–57, Aug., 1955. 1 ref.

The author begins by pointing out that ACTH (corticotrophin) is not a specific remedy for asthma or its allergic component, but only produces a remission of varying duration. The hormone acts by stimulating the function of the adrenal cortex and has also a spasmolytic action.

In clinical use for the treatment of bronchial asthma the author found that, providing there were no contraindications such as tuberculosis, hypertension, marked arteriosclerosis, or ulcerative disease, the administration of small or moderate doses of the hormone (20 to 40 units in 24 hours) caused no notable side-effects within 2 to 3 weeks. Palpitations, tachycardia, restlessness, insomnia, and headache were observed in only 2 out of a large number of patients.

The author states that the most striking advantage of ACTH over other spasmolytic agents such as adrenaline or ephedrine is the favourable action which it exerts on the patient's general health. The hormone is very useful in treating status asthmaticus or in cases in which repeated injections of adrenaline are contraindicated.
H. W. Swann

Corrections

In the issue for August, 1955, page 120, Abstract 400:
(1) After the word "aerosol" in the fourth line of the second paragraph insert "with the exception of narcotine, which was the only compound so far tested which suppressed both the cough excited by simple irritants and that excited by the antigen aerosol".
(2) The authors' observations on the antihistaminic drug "phenergan" (promethazine) were confined to its effect against the cough produced by simple irritants, the only antihistaminic drug tested against the other type of cough being mepyramine maleate. Moreover, although the data provided in the paper appeared to the abstracter to suggest that this drug was more effective than cortisone, no such conclusion was in fact reached by the authors as was attributed to them in the abstract.—EDITOR.

Nutrition and Metabolism

652. Effect of Prolonged Antibiotic Administration on the Weight of Healthy Young Males

T. H. HAIGHT and W. E. PIERCE. *Journal of Nutrition* [*J. Nutr.*] **56**, 151–161, May 10, 1955. 1 fig., 8 refs.

A number of U.S. Navy recruits aged about 18½ years were distributed at random into three groups of just over 100 each, one being given 250 mg. of aureomycin, another 100,000 units of procaine penicillin, and the third tablets of calcium carbonate as a placebo daily by mouth. The tablets were identical and neither observers nor subjects knew the identity of the groups. Height and weight were recorded at the start of the investigation and after 4 and 7 weeks. At the end of the period all three groups had increased in average weight and in weight related to age and height, but the increase had been significantly greater in the two groups given antibiotics than in the control group. The average gains in weight were: with aureomycin, 4·8 lb. (2·7 kg.); with penicillin, 4·1 lb. (1·9 kg.); and with the placebo, 2·7 lb. (1·22 kg.).

To determine whether other factors could account for such differences, a further 242 recruits were divided into three groups and studied similarly except that no drugs were given. [Unfortunately these men were studied at a different time of year and differed from the first batch in that none of them received tablets of any sort; to be truly comparable all should have received the placebo.] There were no significant differences between the groups in weight-gain—which in fact was negligible in all three, this being attributed to the season of the year.

[No explanation is offered for this very interesting observation of the effect of aureomycin and penicillin on weight-gain in young men.] *H. M. Sinclair*

653. The Metabolism of Nitrogen, Calcium and Phosphorus in Undernourished Children. 1. Adaptation to Low Intake of Calories, Protein, Calcium and Phosphorus. 2. The Effect of Supplementary Groundnut-milk Curds on the Metabolism of Nitrogen, Calcium and Phosphorus

H. B. N. MURTHY, S. K. REDDY, M. SWAMINATHAN, V. SUBRAHMANYAN, and G. SUR. *British Journal of Nutrition* [*Brit. J. Nutr.*] **9**, 203–209 and 210–215, 1955. 26 refs.

These papers report work undertaken at the Central Food Technological Research Institute, Mysore, India, to amplify the exceedingly meagre information available on the metabolism of undernourished children. In the first paper the authors report investigations made on 5 undernourished girls aged 7 to 9 years in an orphanage in Mysore. [From the heights and weights given it seems that they were some 6 inches (15·25 cm.) shorter and 15 to 20 lb. (6·8 to 9·2 kg.) lighter than English children of the same age.] Their diet was completely vegetarian and nearly 80% of the daily intake of 1,010 Calories came from rice. Their mean 24-hour basal metabolism, as calculated from tables (with a reduction of 15% since the basal metabolic rate of the average Indian seems to be lower than the standard value by this amount), was 718 Calories, so that their consumption of calories was only 40% more than the basal requirement. In contrast, in healthy American children caloric intake has been shown to be 90 to 100% above the basal standard. More work is clearly needed on the basal metabolism and energy requirements of undernourished children.

The average intake of nitrogen was only 3 g., yet all the children were in positive nitrogen balance, with a mean retention of 0·28 g. The intake of calcium was also low, the average being 200 mg., yet the average retention was 23 mg., although one of the five was in negative calcium balance. Similarly, the average intake of phosphorus was 567 mg. and the average retention 62 mg., with one child in negative balance. Apart from their intrinsic interest, these figures support the view expressed by other workers that a process of adaptation to low levels of intake of certain nutrients may occur.

The second paper describes work carried out to amplify the previous finding of Subrahmanyan *et al.* (*Brit. J. Nutr.*, 1954, **8**, 348) in undernourished children that supplementation of a poor rice diet with ground-nut milk curd for 6 months produced a striking improvement in growth and nutritional status. The authors have now studied the effect of this supplement on the metabolism of nitrogen, calcium, and phosphorus in 6 girls of 8 to 11 years, each of whom was paired with another of comparable age, weight, and height for control purposes. The average retention of all three elements was increased by the supplement—nitrogen from 0·28 to 0·73 g., calcium from 73 to 233 mg., and phosphorus from 57 to 116 mg. The authors suggest that ground-nut preparations might go a long way to make up deficiencies in diet in India, where scarcity and high cost make it difficult to increase milk consumption. *John Yudkin*

654. Studies on Agammaglobulinemia. II. Failure of Plasma Cell Formation in the Bone Marrow and Lymph Nodes of Patients with Agammaglobulinemia

R. A. GOOD. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 167–181, Aug., 1955. 8 figs., 32 refs.

The morphology of the bone marrow and lymph nodes and the effect on it of antigenic stimulation were studied at the University of Minnesota, Minneapolis, in 4 patients with electrophoretically confirmed agammaglobulinaemia and in 12 essentially normal children aged 6 to 12 years. The patients were 2 boys, both aged 7 years, with the congenital form of the disease, and 2 adults, a woman aged 30 and a man aged 58, with the acquired form which was of several years' duration. In the

normal children the number of plasma cells per 5,000 nucleated cells in the bone marrow ranged from 11 to 32 (mean 19·8); in 15 normal adults aged 18 to 41 years the number ranged from 8 to 61 per 5,000 nucleated cells (mean 31·0). In none of the 4 patients was there more than one plasma cell per 5,000 nucleated cells in the bone marrow. Intensive stimulation with T.A.B. vaccine resulted in a fivefold increase in the number of plasma cells in the bone marrow of 4 normal children who acted as controls, but little or no change in the 4 patients. The controls developed typhoid H-agglutinin titres greater than 1 in 10,000, whereas the patients with agammaglobulinaemia produced no H agglutinin at all. Similar findings resulted from stimulation with other antibodies, such as virus antigens, diphtheria and tetanus toxoids, and heterologous erythrocytes.

The lymph nodes of all 4 patients showed a relative thinness of the cortex, deficiency of primary lymph follicles, an increase in fibrous tissue and reticulum, and the entire absence of plasma cells, although small numbers of these cells were regularly found in the lymph nodes of normal children. Following primary exposure to T.A.B. vaccine, the response in the normal subjects included proliferation of the lymphocytes and reticulum cells, formation of secondary follicles, and an increase in the number of plasma cells. In the patients, on the other hand, the same type of stimulation produced some proliferation of lymphocytes and reticulum cells, but no plasma cells could be found and there were no secondary lymph follicles. These differences became more marked after secondary exposure to T.A.B. vaccine, plasma cells becoming abundant in the normal subjects but remaining absent in the patients. *M. Lubran*

655. **The Clearance of Uric Acid in Normal and Gouty Subjects.** (La clearance dell'acido urico nel soggetto normale e nel gottoso)

G. Sala, C. B. Ballabio, and A. Amira. *Reumatismo* [*Reumatismo*] 7, 223–228, July–Aug., 1955. 22 refs.

At the Medical Clinic of the University of Milan the authors investigated the renal function in regard to uric acid of 30 healthy and 9 hyperuricaemic gouty subjects. The uric acid clearance was determined and at the same time the glomerular filtration rate was estimated by the endogenous creatinine method and the sodium thiosulphate method.

Their results provide support for the hypothesis that a renal factor is involved in the pathogenesis of hyperuricaemia in gout. The mean value for uric acid clearance in the normal subjects was $9{\cdot}25 \pm 0{\cdot}75$ ml. per minute, and in the gouty subjects $3{\cdot}59 \pm 0{\cdot}3$ ml. per minute, the difference being highly significant statistically. A relationship was observed between uric acid clearance and urinary flow, the former decreasing even in normal subjects when the latter was less than 1 ml. per minute.

In 4 gouty subjects there was a marked reduction in the glomerular filtration rate; the mean uric acid clearance in these cases was $3{\cdot}40 \pm 0{\cdot}44$ ml. per minute, whereas in the remainder it was $3{\cdot}87 \pm 0{\cdot}43$ ml. per minute. *E. Forrai*

656. **The Effect of Intravenous Demecolcine (Colcemid) on Acute Gout**

W. C. Kuzell, R. W. Schaffarzick, and W. E. Naugler. *Archives of Internal Medicine* [*Arch. intern. Med.*] **96**, 153–156, Aug., 1955. 7 refs.

Demecolcine ("colcemid"), an alkaloid from the meadow saffron, differing from colchicine structurally in the replacement of the acetyl by a methyl radical, was given intravenously to a series of 20 patients with acute gout. Of the 20 patients, 15 enjoyed complete remission within 48 hours after the administration of 1 to 4 mg. of demecolcine. Four other subjects were afforded partial amelioration of signs and symptoms. The only undesirable side-action was the occurrence of diarrhea in 2 of the 20 patients.—[Authors' summary.]

657. **Effect of ACTH and Cortisone on Fat Absorption in Steatorrhea of Various Causes**

E. J. Drenick, E. Hvolboll, and J. A. Halsted. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 303–308, Aug. 25, 1955. 3 figs., 18 refs.

The effect of ACTH and cortisone on fat absorption in steatorrhoea other than that caused by non-tropical sprue was studied at the Veterans Administration Center, Los Angeles, the following 4 cases being chosen for this purpose: (1) steatorrhoea associated with subtotal gastrectomy and gastrojejunostomy; (2) extensive ileojejunitis with severe secondary malabsorption; (3) pancreatic calcinosis and pancreatic insufficiency; and (4) severe non-tropical sprue. The fat balance was ascertained during 2 to 4 preliminary control periods of 5 days each. Intramuscular injections of ACTH and cortisone were then given for 9 to 20 periods of 5 days each, the dosage of ACTH being 40 to 200 mg. daily and of cortisone 50 to 250 mg. daily. In addition to fat balance estimations in all cases the nitrogen balance was determined in Cases 1 and 3. Laboratory estimations included complete blood count, eosinophil count, serum electrolyte values, and blood sugar and blood urea nitrogen levels during every period of study. Stools were collected in 5-day pools and the fat content estimated. During every other period a representative 24-hour diet sample was analysed for fat and nitrogen.

No decrease in faecal fat was observed in Case 1, that of a man of 56, during 2 periods of cortisone and 5 periods of ACTH treatment, but there was a negative nitrogen balance during administration of ACTH. In Case 2, that of a man of 30, a moderate decrease in steatorrhoea from 50 to 25% was noted during cortisone and ACTH therapy, this being concomitant with clinical improvement. There was improvement in Case 3 with administration of pancreatic extract but not with cortisone, on which the patient, a man of 58, went into negative nitrogen balance. In Case 4, that of a woman of 29, administration of cortisone resulted in marked clinical improvement, with reduction of faecal fat from 84 to 25%.

The authors consider that the improvement noted in 2 cases may reflect a general metabolic restoration rather than a specific effect on the absorptive capacity of the intestine. *Norval Taylor*

Gastroenterology

658. **The Relation between Sideropenia and Anemia and the Occurrence of Postcibal Symptoms following Partial Gastrectomy for Peptic Ulcer**
S. WALLENSTEN. *Surgery* [*Surgery*] **38**, 289–297, Aug., 1955. 20 refs.

The author, at Serafimerlasarettet, Stockholm, attempted to determine whether there was any relationship between sideropenia and post-gastrectomy symptoms in a series of 587 patients, of whom 148 (104 males and 44 females) had been subjected to the Billroth-I type of partial gastrectomy and 439 (321 males and 118 females) to the Billroth-II or Polya type. Symptoms were graded, and in each case the serum iron level was determined by the method of Agner and the haemoglobin content with a photoelectric colorimeter. The lower limit of the normal serum iron level was taken as 60 to 70 μg. per 100 ml.

It was found that the incidence of post-gastrectomy symptoms was highest in females who had undergone a Polya gastrectomy. Statistical analysis showed that post-cibal symptoms occurred more frequently in patients with a low serum iron level than in those with a normal serum iron level. Severe symptoms were often associated with a haemoglobin value of less than 9·8 g. per 100 ml. in women and less than 11·5 g. per 100 ml. in men. It was also found that the incidence of post-cibal symptoms was related to the degree of iron deficiency. When a preparation of iron was given intravenously to 21 patients with sideropenia and 6 with a normal serum iron level there was improvement in symptoms in all except one.

[This is an excellent paper, but the time at which the serum iron values were determined is not stated; the serum iron level varies with meals and there is a very definite diurnal variation.] *I. McLean Baird*

659. **The Gastric Secretory Response to Histalog: One-hour Basal and Histalog Secretion in Normal Persons and in Patients with Duodenal Ulcer and Gastric Ulcer**
J. B. KIRSNER and H. FORD. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 307–311, Aug., 1955. 2 refs.

In an investigation at the University of Chicago the gastric secretory response to histalog (3-β-aminoethyl pyrazole), an analogue of histamine, in a dosage of 0·5 mg. per kg. body weight was studied in 584 healthy subjects and 253 patients with peptic ulcer. Basal secretion was recorded at 15-minute intervals for one hour; histalog was then administered and the recordings were repeated for a second hour. Basal secretion was considerably higher in the 231 patients with duodenal ulcer than in healthy subjects, especially in women. Anacidity was noted in the basal secretion in only 2 patients in this group, as against 22% of 304 healthy males and 30% of 280 healthy females. The response to histalog in cases of duodenal ulcer was similar to that in healthy subjects. Basal secretion and the response to histalog in patients with gastric ulcer approximated to normal. The finding of a significantly higher secretion in cases of duodenal ulcer over the one-hour period confirms the findings of others over the 12-hour nocturnal period. *Thomas Hunt*

660. **The Post-cholecystectomy Syndrome**
E. SAMUEL. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 482–494, Sept., 1955. 11 figs., 17 refs.

Cholecystectomy in animals is followed by dilatation of the bile ducts, but it is problematical whether this occurs in man. With improved radiological technique in recent years it has been shown that although in many cases there is no significant dilatation of the ducts after cholecystectomy, in others—notably cases of gall-bladder disease—the ducts may be dilated before operation. When, therefore, postoperative dilatation does occur it is more likely to indicate a pathological change than a compensatory phenomenon.

In this paper an analysis is presented of the clinical and radiological findings in 36 cases of the "post-cholecystectomy syndrome". Before examination a high colonic lavage was carried out in order to eliminate gas and faeces from the hepatic flexure. An intravenous injection of 40 ml. of "biligrafin" was given and radiographs were taken at 15 and 40 minutes. Tomography was found to be of considerable value in differentiating stones in the common duct from overlying gas shadows in the duodenum.

Clinically, the commonest presenting symptom was pain, which was of two main types. (1) A severe colicky type of pain in the right hypochondrium sometimes radiating into the back, and considered to be almost diagnostic of stone formation; in 6 out of 11 patients complaining of this type of pain stones were demonstrated in the common bile duct, while the choledochogram in the other 5 showed direct or indirect evidence suggestive of some obstruction. (2) Right hypochondrial pain, which was severe and intermittent but not colicky; in 2 of the 10 patients with this type of pain there was dilatation of the common bile duct; in the others the ducts were normal and pain was not considered to be of biliary origin. Distension and flatulence were the next most frequent symptoms (13 cases), but the bile ducts were normal in appearance. Attacks of jaundice were noted in only 4 patients; in one of these the bile ducts were normal, in 2 they were dilated, and in one there were two stones in the cystic duct. Indigestion, which was present in 6 cases before operation, was unaffected. Many patients had more than one of these symptoms, some of which, though attributed to the cholecystectomy, were considered to be due to other causes.

The lower end of the common bile duct passes through the pancreas and is usually difficult to see; the "funnel-shaped tapering shadow" which fades out is regarded as normal. In the absence of obstruction the opaque

medium can be seen in the duodenum within 15 to 40 minutes. It may also pass back into the duodenal bulb, giving rise to a shadow which may be mistaken for a gall-bladder shadow. When, however, there is obstruction at the sphincter of Oddi, the common bile duct becomes dilated (diameter over 12 mm.), and has a " cigar-shaped " termination extending up to the medial wall of the duodenum. In the 3 cases in this series in which there was thought to be obstruction at the sphincter of Oddi the medium did not appear in the duodenum within 2 hours and inhalation of octyl nitrite did not relieve the obstruction. It is doubtful, therefore, whether the obstruction was due to spasm. Cystic-duct remnants were found in 8 cases, and were considered to be responsible for the symptoms in 3 of these.

[This paper is well worth reading in the original.]

G. Ansell

661. **Prevalence and Nature of Hepatic Disturbance following Acute Viral Hepatitis with Jaundice**

J. R. Neefe, J. M. Gambescia, C. H. Kurtz, H. D. Smith, G. W. Beebe, S. Jablon, J. G. Reinhold, and S. C. Williams. *Annals of Internal Medicine* [*Ann. intern. Med.*] **43**, 1–32, July, 1955. 5 figs., 21 refs.

This detailed and careful study, which forms part of a wider investigation initiated by the U.S. National Research Council, was undertaken at the University of Pennsylvania Medical School, Philadelphia, primarily to determine the ultimate prognosis of viral hepatitis. Three groups of subjects were investigated: (1) a " post-hepatitis " group composed of 271 persons who had suffered from viral hepatitis with jaundice 2 to 7 years previously; (2) a " heavy exposure " group consisting of 138 ex-servicemen who had been in camps where there had been an unusually high incidence of hepatitis; and (3) a " minimal exposure " group, which acted as a control group, totalled 271 and included soldiers not unduly exposed to viral hepatitis and healthy medical students, the average age being therefore lower than in the other two groups. Many of the subjects in each group were subjected to a large variety of liver function tests, including measurements of serum bilirubin level, flocculation and turbidity tests, serum protein and phosphatase estimations, measurement of prothrombin time, and the " bromsulphalein " test. Needle biopsy of the liver was carried out on 11 persons who appeared to have hepatic disease.

The liver function tests gave abnormal results most frequently in Group 1, and least in Group 3. On the other hand it appeared improbable that viral hepatitis was responsible for all the abnormalities noted in Group 1, at least three aetiological agents being diagnosed by biopsy. About 5% of the control group showed abnormalities of liver function, and the significance of this is discussed. The authors conclude that the occurrence of an episode of hepatic disease more than 3 years after viral hepatitis (during which there have been no symptoms) is probably due to another disease process, and that in such cases liver biopsy examination may be required to determine the cause of the later attack.

W. H. Horner Andrews

662. **Post-hepatitis Hyperbilirubinaemia. (So-called Acquired Haemolytic Anaemia following Hepatitis.)** (Die posthepatitsche Hyperbilirubinämie. (Der sog. erworbene hämolytische Ikterus nach Hepatitis))

H. Kalk and E. Wildhirt. *Zeitschrift für klinische Medizin* [*Z. klin. Med.*] **153**, 354–387, 1955. 2 figs., bibliography.

This long paper from the City Hospital of Kassel, Germany, deals with a condition described by the senior author in 1947 as " acquired haemolytic jaundice following hepatitis ", but for which the term " post-hepatitic bilirubinaemia " is now preferred. The authors point out that cirrhosis of the liver is universally recognized as a sequel in some cases of acute infective hepatitis, but that other sequelae such as the one they describe are not well known to clinicians.

The present paper is based on the findings in 115 cases (including 38 previously described elsewhere). All the patients had had infective (epidemic) hepatitis with jaundice, and all later showed persistent bilirubinaemia (positive indirect van den Bergh reaction) without a trace of bile pigment in the urine. There was no evidence of haemolysis, no increased osmotic fragility of erythrocytes, and no excess of reticulocytes in the blood. The spleen was just palpable in most cases. In 64 cases biopsy of the liver was performed, and in no case was any sign of inflammation found in the liver. A brown, iron-free pigment, which was certainly not bile pigment, was abundant in both Kupffer and liver cells. The prognosis is good, and in no patient did any anaemia ensue. One patient has been observed for 12 years. Liver function tests generally give normal results.

The authors have no rational explanation to offer for the development of persisting bilirubinaemia as a sequel to acute infective hepatitis—nor indeed had previous authors who have described the condition. Pigment metabolism in the liver is obviously abnormal, but this seems to do no real harm.

J. W. McNee

663. **Acute and Subacute Ileitis.** (Les iléites aiguës et subaiguës)

—. Chérigié, —. Tavernier, —. Dupas, and —. Raynal. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **44**, 583–597, May, 1955. 12 figs.

The authors, working at the Hôpital Claude-Bernard, Paris, have made radiological studies of the ileocaecal region of 70 patients, mostly children, with infectious diseases (measles, scarlet fever, Vincent's angina, or pneumonia) presenting with abdominal pain and tenderness simulating acute appendicitis, and of 9 healthy children. The terminal ileum was studied after barium meal or enema (usually the latter) with the help of abdominal compression. In only 3 of the healthy children were lymph follicles seen, and all 3 were *Ascaris* carriers. On the other hand 80% of the patients had obvious hypertrophy of the lymph follicles and Peyer's patches, together with enlargement of the mesenteric lymph nodes. The abnormality usually disappears after a few days; if it persists, Crohn's disease or ileocaecal tuberculosis should be suspected.

P. C. Reynell

Cardiovascular System

664. **Thromboangeitis Obliterans. Clinical and Arteriographic Findings, with a Discussion on Clinical Diagnosis**
G. E. MAVOR. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 229–243, July, 1955. 20 figs., 22 refs.

The distinction between thromboangiitis obliterans and arteriosclerosis has not always been clear and the differential diagnosis has often depended mainly on the age of the patient. In a recent study carried out at the Royal Infirmary, Aberdeen, of 162 patients with ischaemic vascular disease of the lower limbs the author concluded that 4 had thrombosis secondary to trauma, 149 had atheroma with secondary thrombosis, 3 had arterial embolism, and 6, whose cases are described in detail, had true thromboangiitis obliterans.

He confirms Buerger's opinion that the condition is a distinct clinical entity which occurs in young adults, seldom beginning after the age of 35; it affects first the digital or plantar arteries and then ascends, though it seldom reaches the popliteal arteries. Veins are involved at the same time in about one-sixth of all cases. The presence of obstruction of large vessels and local acute arteritis are against the diagnosis of angiitis obliterans. While the disease is unilateral to begin with, it invariably becomes bilateral; one of its most striking features is its periodicity, the attacks varying in intensity and duration. The author holds that the disease is typically one of small vessels, and that it is characterized clinically by claudication of the arch of the foot rather than claudication of the calf, these views being supported by arteriographic findings. The non-specific histological character of the changes in the vessels has led to erroneous diagnoses and much harm in the past.

The cause of the disease remains unknown and treatment is therefore mainly palliative. Lumbar ganglionectomy is always indicated, but amputation, even in the presence of gangrene, should not be undertaken hastily.

J. McMichael

665. **Idiopathic Dilatation of the Pulmonary Artery**
F. S. P. VAN BUCHEM, J. NIEVEEN, W. MARRING, and L. B. VAN DER SLIKKE. *Diseases of the Chest* [*Dis. Chest*] **28**, 326–336, Sept., 1955. 8 figs., 14 refs.

In the 5 cases of idiopathic dilatation of the pulmonary artery here described from the University of Groningen, Netherlands, there was no increase in pulmonary flow such as occurs in atrial or ventricular septal defect, patent ductus, or anomalous venous return, no pulmonary hypertension, and no valvular pulmonary stenosis. The ventricular and pulmonary pressures were equal and within the normal range. The oxygen saturation was normal. Angiocardiography was used in these cases to determine the diameter of the pulmonary artery, which ranged from 39 to 49 mm.

C. W. C. Bain

666. **Myocarditis: a Clinical and Pathologic Study of Forty-five Cases**
M. J. LUSTOK, J. CHASE, and J. M. LUBITZ. *Diseases of the Chest* [*Dis. Chest*] **28**, 243–259, Sept., 1955. 13 figs., 15 refs.

In this paper from Marquette University School of Medicine and the Veterans Administration Hospital, Wood, Wisconsin, 45 cases of myocarditis unassociated with rheumatic or hypertensive heart disease are described. In 8 cases the condition was fulminating and progressed rapidly. On the other hand in 4 benign cases the patient had no cardiac symptoms, the diagnosis being made only from the electrocardiographic abnormalities found during some febrile disorder. In 20 cases the patient presented with congestive cardiac failure. In 4 cases anasarca recurred after an interval, requiring further hospital treatment, while in 9, of which 5 were fatal, it never cleared completely. Necropsy was carried out in 10 cases and showed areas of focal necrosis in the fulminating cases and interstitial oedema with dilated ventricles and subendocardial fibrosis in the more chronic types.

[Although a history of chronic alcoholism was obtained in half of these cases vitamin B does not appear to have been given. In some of the patients who recovered, the evidence, clinical, electrocardiographic, and radiological, would seem to point more to pericardial effusion than to myocarditis, suggesting that the latter condition may not be so common as this paper would lead one to suppose.] *C. W. C. Bain*

667. **Prolonged Survival in a Case of Septic Endocarditis.** (О хроническом течении септического эндокардита)
E. N. SOLOMINA. *Советская Медицина* [*Sovetsk. Med.*] 33–38, No. 8, Aug., 1955.

The author describes a case of septic endocarditis in which the patient has survived numerous recurrences since its onset at least 7 and possibly 9 years ago. The patient is a woman, now aged 57, whose childhood was spent in very poor conditions; she suffered at the age of 12 from joint pains and had oral sepsis at 19. After she had married and had 3 children she developed recurrent typhus, followed by frequent quinsies for 2 years. Her first child was born naturally, but at the other two confinements labour was artificially induced, and she developed chronic infection of the adnexa. At 26 she had appendicitis and colitis, and underwent appendicectomy. At the age of 37 she developed dyspnoea and palpitation on exertion, and 2 years later heart disease was diagnosed. From the age of 40 she was unable to work, suffering also from uterine haemorrhages. She first came under observation by the present author in 1946 with duodenal ulceration and aortic and mitral valvular disease. The diagnosis of septic

endocarditis was not made until 1948; she was then given a course of penicillin totalling 20 mega units and her condition improved. However, between 1948 and 1955 she has been in hospital 12 times, and has received in all 136 mega units of penicillin and 11 g. of streptomycin.

The strangest thing about the clinical history of this unfortunate woman is that she did not develop congestive heart failure until the end of 1954, and even then responded to antibiotics and strophanthin. The chief pathogenic organism cultured from her blood was usually *Streptococcus viridans*, but on one occasion a pathogenic staphylococcus was isolated. Another remarkable feature of the case is that syphilis was suspected in 1945, but at the time the Wassermann reaction was negative; between 1949 and 1951 it was strongly positive, but later became negative again. The author rejects the diagnosis of syphilis and regards the positive reaction as non-specific. The patient was still alive at the time of the report. *L. Firman-Edwards*

CONGENITAL HEART DISEASE

668. **Pulmonary Stenosis and Interatrial Communication with Cyanosis. Hemodynamic and Clinical Study of Ten Patients**

J. A. CALLAHAN, R. O. BRANDENBURG, and H. J. C. SWAN. *American Journal of Medicine* [*Amer. J. Med.*] **19**, 189–202, Aug., 1955. 5 figs., 32 refs.

At the Mayo Clinic the authors have studied a series of 10 cases of pulmonary stenosis with interatrial communication, right-to-left shunt, and cyanosis. Clinical details of these cases are briefly given and summarized in tabular form, and their similarity to those of the tetralogy of Fallot is noted. Cyanosis had been present from birth in 8 of the 10 cases. The investigations included cardiac catheterization with measurement of intracardiac and systemic arterial pressure, and determination of the oxygen content and the oxygen capacity of systemic arterial blood. For the recognition of possible small left-to-right shunts determination of the oxygen saturation of multiple small blood samples obtained from the various cardiac chambers was carried out. The difference between pulmonary and systemic blood flow, calculated according to Fick's principle and expressed as the percentage of systemic flow, indicated the degree of right-to-left shunt present. Dye-dilution curves were recorded after the injection of azovan (Evans) blue into the cardiac chambers and great vessels at different times.

In all cases the right ventricular pressure was found to be elevated, and in 6 it exceeded that in the radial artery. Similarly the blood oxygen capacity was increased, pulmonary blood flow was less than systemic, and the right-to-left shunt was large in all cases; and in no case was there any evidence of a left-to-right shunt. Dye-dilution curves confirmed the presence of a right-to-left shunt through an interatrial communication. Pulmonary valvotomy was carried out on 9 patients, 3 of whom died shortly after operation; varying degrees of improvement were noted in the surviving patients. Studies performed during operation showed that the right ventricular pressure fell after valvotomy.

The differential diagnosis between this condition and the tetralogy of Fallot is difficult on clinical grounds. The distinction can, however, be made with the combined help of cardiac catheterization and dye-dilution curves from various sites of injection. The cardiac malformations in these cases are potentially curable, and many authorities advise treatment by pulmonary valvotomy rather than by a shunt operation.

Francis Page

669. **Atypical Tetralogy of Fallot: a Noncyanotic Form with Increased Lung Vascularity. Report of Four Cases**

R. D. ROWE, P. VLAD, and J. D. KEITH. *Circulation* [*Circulation* (*N.Y.*)] **12**, 230–238, Aug., 1955. 7 figs., 34 refs.

The cases of 4 infants are reported from the Hospital for Sick Children, Toronto, in whom pulmonary stenosis of moderate degree was associated with a large ventricular septal defect and a large left-to-right shunt. Cyanosis was absent in all these cases and the main symptoms were failure to thrive and frequent respiratory infections. On cardiac catheterization it was found possible to enter the aorta from the right ventricle in 3 cases. The right ventricular pressure equalled the systemic systolic level, and arterial oxygen saturation was normal both at rest and after exercise. In one case that came to necropsy the aorta overrode the septal defect, and the condition was clearly an example of the tetralogy of Fallot. Radiology revealed pulmonary plethora, and angiocardiography showed that the aorta filled at least one second after the pulmonary artery.

The authors suggest that cases such as these, in which there is evidently an increased pulmonary blood flow, should be looked upon as variants of the tetralogy not requiring the usual operative procedures. Any surgical treatment should be directed towards correction of the septal defect. *James W. Brown*

670. **Surgical Correction of Tetralogy of Fallot. Results in First One Hundred Cases Six to Eight Years after Operation**

W. J. POTTS, S. GIBSON, E. BERMAN, H. WHITE, and R. A. MILLER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 95–99, Sept. 10, 1955. 5 refs.

The authors here give details of the long-term results of aortic–pulmonary anastomosis for Fallot's tetralogy in the first 100 cases so treated at the Children's Hospital, Chicago, since 1946. All the patients were under 16 years of age and 35 were less than 4. Before operation 60 were classed as "bad-risk cases". The standard Potts operation was performed in all but one case, in which a subclavian–pulmonary anastomosis had to be carried out as the pulmonary artery was very short. At first a 5-mm. anastomosis was made, but this was soon reduced to 4 mm. except in very young children. A second operation was necessary in 4 cases, but in only one—the case in which a subclavian–pulmonary anasto-

mosis was performed—had the anastomosis become occluded. The operative mortality was 9%, a disproportionate number of deaths occurring among the youngest patients.

The difficulties in evaluation of the results are stressed. The authors have undertaken a very careful follow-up, and have assessed the patients on clinical grounds. They have demanded a high standard before classifying a result as "good", but despite this they have felt justified in placing 68% in this group, while in 16% the result was classified as "fair". Cardiac enlargement has occurred in many patients, but its extent has not been closely related to the clinical result, and although it has often occurred soon after operation, it has not been progressive. There have been 5 late deaths, only one of which was due to a cardiac cause.

J. R. Belcher

DISTURBANCES OF RHYTHM AND CONDUCTION

671. **Precipitation of Ventricular Arrhythmias due to Digitalis by Carbohydrate Administration**

E. PAGE. *American Journal of Medicine* [*Amer. J. Med.*] 19, 169–176, Aug., 1955. 7 figs., 18 refs.

Potassium depletion has been shown to predispose to the development of cardiac manifestations of digitalis intoxication and to enhance cardiac arrhythmia when already present. As electrocardiographic changes resembling those of potassium deficiency may occur after meals (and are thought to be due to dietary carbohydrate) the author has investigated the possibility of a relationship between carbohydrate metabolism and clinical digitalis intoxication.

At the Jefferson-Hillman Hospital (Medical College of Alabama), Birmingham, Alabama, 37 patients receiving digitalis in various dosages were studied in the fasting state, serial electrocardiograms (ECGs) being taken before and after giving a dose of 100 g. of glucose by mouth. Intravenous glucose or a high-carbohydrate meal was occasionally given in place of the oral dose of glucose. Ventricular arrhythmias were precipitated by this procedure on 15 occasions in 7 cases, which are described in some detail, with illustrations showing examples of the changes in the ECG.

The clinical implications of these findings, which the author attributes to a reduction in the serum potassium level, are discussed. The possibility that serious arrhythmias may be precipitated in digitalized patients by the administration of carbohydrate is of some importance, especially in cases of vomiting resulting from overdosage of digitalis, in which infusions of glucose solution may be the chief means of sustaining adequate nutrition, and in patients with recent myocardial infarction. The author tentatively suggests that as a measure of prophylaxis digitalized patients should be given potassium salts together with carbohydrate feeds, that their total carbohydrate intake should be restricted, and that excessive emotional disturbance and hypoglycaemia, both of which may reduce the serum potassium level, should be avoided.

Francis Page

672. **Diastolic Overload in Mechanical Ventricular Alternans**

S. M. SANCETTA. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] 46, 342–347, Sept., 1955. 3 figs., 8 refs.

Observations made at the City Hospital (Western Reserve University), Cleveland, Ohio, on a patient with decompensated aortic stenosis, on whom cardiac catheterization and jugular bulb puncture were performed during mild exercise, demonstrated that the mechanical pulsus alternans which was produced by the exercise occurred over a critical range of increased ventricular end-diastolic pressures. It was noted that alternation appeared even when there was no change in the venous return, and persisted in spite of a measurable increase in the latter.

The author suggests that the findings recorded in this case emphasize the fact that directional changes in venous return are not as important a factor in the onset and disappearance of pulsus alternans as are the changes in ventricular end-diastolic pressure and, by inference, end-diastolic volume and initial stretch. He admits that the data presented do not dissociate primary myogenic changes from haemodynamic factors in the genesis of ventricular alternans, but do support the thesis that changes in diastolic overload are of importance and that they may be independent of myogenic factors.

William A. R. Thomson

CHRONIC VALVULAR DISEASE

673. **The Significance of Previous Embolism for the Prognosis of Commissurotomy for Mitral Stenosis.** (Il significato prognostico delle embolie di fronte alla commissurotomia per stenosi mitralica)

A. ACTIS-DATO and F. MORINO. *Minerva medica* [*Minerva med.* (*Torino*)] 2, 255–263, Aug. 4, 1955. Bibliography.

A review of the histories of 500 cases of mitral stenosis in which commissurotomy was performed at the University Cardiac Surgery Centre, Turin, showed that 52 patients (10%) had experienced embolic episodes preoperatively. At operation embolism was observed in 5 other patients, of whom 3 had died, and subsequently a further 14 patients suffered embolism which proved fatal in 3.

The authors have modified their previous view that operation should be deferred for at least 6 months in the presence of embolism, and now advise early operation in spite of this event, although such patients are at greater risk, embolism occurring in 11·5% of them as against only 3% of the remaining 448 cases, and resulting in a mortality of 5·7% as against 0·67%. In none of the 49 patients previously experiencing embolism and surviving operation has there been further evidence of this complication.

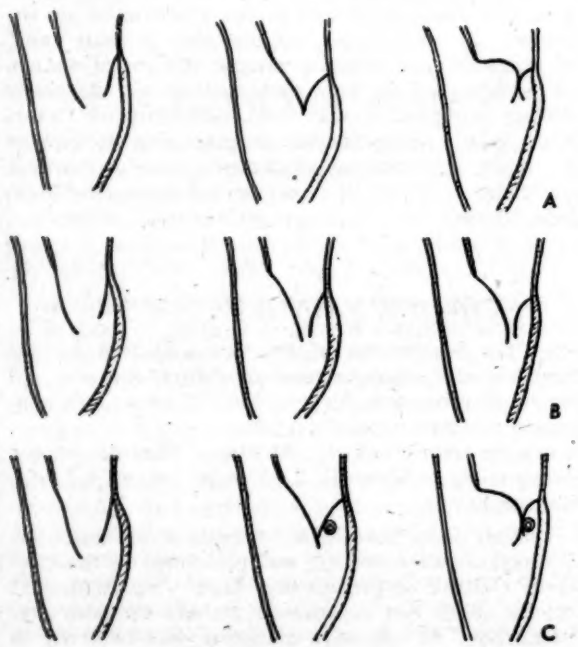
The authors express the view that with exclusion of the auricle and the improvement in cardiac function the patient is protected against further episodes of this kind.

C. A. Jackson

674. A Surgical Approach to the Correction of Mitral Insufficiency

S. SAKAKIBARA. *Annals of Surgery* [*Ann. Surg.*] **142**, 196–203, Aug., 1955. 4 figs., 7 refs.

The author, working at the Tokyo Women's Medical College, has studied the mechanics of mitral regurgitation in experimental animals and in human subjects at operation and post mortem, and postulates that the condition is often due to failure of the posterior cusp to rise sufficiently to meet the anterior cusp, being prevented by adhesions between the chordae tendineae and the ventricular wall and by cicatrization of the chordae themselves (see figure). The reflux of blood therefore takes place through the posterior part of the mitral ring, as can be confirmed by palpation at operation, the regurgitation being reduced to a minimum when the surgeon's finger is placed on the auricular surface of the posterior cusp so as to protrude approximately 3 mm. into the ring.



Schematic diagram of: (A) Normal mitral valve. (B) Mitral valve in regurgitation. (C) Mitral valve following operation.

On the basis of these observations the author has devised an operation designed to correct the valve deformity by elevating the posterior cusp so that the much larger anterior cusp makes contact with it on ventricular systole. The valve is first explored and valvotomy performed if necessary. If regurgitation is excessive and seems capable of correction, the incision is enlarged so as to allow the heart to be manipulated freely. Meanwhile a length of saphenous vein is excised, turned inside out, and several strands of stout silk, braided together, passed through it. (The purpose of the vein is merely to act as a covering for the silk sutures, to which it is fixed at either end.) With one finger in the heart, the surgeon now inserts a probe carrying the silk sutures through the anterior wall into the left ventricle, passing behind the chordae tendineae of the posterior cusp from left to right, and emerging through the posterior ventricular wall, the heart being inverted carefully as the probe is pushed through. The vein-covered braided sutures are then pulled through and anchored to the myocardium at each end, the tension being so adjusted that the posterior cusp is lifted up sufficiently to bring it into contact with the anterior leaf during ventricular systole.

In all, 29 patients have been treated by this method with 2 operative deaths. Clinical improvement has been maintained over a limited follow-up period in most cases.

T. Holmes Sellors

CORONARY DISEASE AND MYOCARDIAL INFARCTION

675. The Surgical Treatment of Cardiac Aneurysm. (Die chirurgische Behandlung des Herzaneurysmas)

F. F. NIEDNER. *Thoraxchirurgie* [*Thoraxchirurgie*] **3**, 93–111, Aug., 1955. 14 figs., 33 refs.

The author has found in the German literature only two accounts of the surgical treatment of aneurysm of the heart; yet, he states, the condition is by no means so uncommon as is often supposed, 38% of myocardial infarctions being followed by cardiac aneurysm, and it has been reported that 7 to 9% of patients with myocardial infarction die of rupture of the heart. In this paper from the Municipal Surgical Clinic, Ulm, the author discusses the possibility of surgical treatment in this condition and points out that even when it is correctly diagnosed, the manifold difficulties and dangers of an operation trespassing upon the coronary arteries and their collaterals, combined with the fact that patients with aneurysm of the heart may live as long as 10 years or more without operation, have not encouraged the development of a surgical approach to this problem.

For ventricular aneurysm excision is not practicable, although in one case it was successfully performed for aneurysm of the auricle which, owing to the absence of vitally important blood vessels, lends itself more readily to resection. In cases which heal naturally there is marked thickening of the pericardium over the aneurysm, and following this lead perhaps the most hopeful method of surgical treatment is to compress and contain the aneurysm by means of a skin graft applied, after removal of the subcutaneous fat, with its outer surface towards the aneurysm. Full details of such an operation are given, together with the clinical history, radiological findings, and electrocardiographic records of 3 cases successfully operated upon in which the aneurysm was situated respectively (1) in the region of the descending branch of the left coronary artery, (2) in the region of the circumflex branch of the left coronary, and (3) at the base of the right auricle.

While it is too early yet to assess the true value of this procedure in these cases, there can be little doubt that the three main dangers of heart aneurysm—namely, fibrillation, embolism, and rupture—are much reduced after operation.

D. P. McDonald

676. **Long-acting Coronary Vasodilator Drugs: Metamine, Paveril, Nitroglyn and Peritrate**
H. I. Russek, B. L. Zohman, A. E. Drumm, W. Weingarten, and V. J. Dorset. *Circulation* [*Circulation (N.Y.)*] **12**, 169–175, Aug., 1955. 5 figs., 4 refs.

The clinical effect in angina pectoris of " metamine " (triethanolamine trinitrate biphosphate), " paveril " (dioxyline phosphate), " nitroglyn " (glyceryl trinitrate in a sustained-action tablet), and " peritrate " (pentaerythritol tetranitrate), all reputed to be long-acting coronary vasodilators, was investigated at the U.S. Public Health Service Hospital, Staten Island, New York. A group of 21 men aged 46 to 69 years with coronary arterial disease in whom the electrocardiographic response to standard exercise (Master two-step test) was relatively constant were selected, and the ability of each drug to modify the electrocardiographic response in repeated tests was noted. It was found that peritrate in doses of 10 to 20 mg. was the only drug which could be properly described as a long-acting coronary vasodilator; in some cases its effects were evident 5 to 6 hours after a therapeutic dose. If peritrate is taken after food its effects may be attenuated or even abolished.

James W. Brown

677. **Studies on Coronary Blood Flow, with Emphasis on the Treatment of Coronary Insufficiency**
W. L. Jamison, L. DeVera, G. Katakis, J. Alai, and H. T. Nichols. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **3**, 521–526, Aug., 1955. 1 fig., 2 refs.

Coronary blood flow was studied in a series of experiments on dogs at the Hahnemann Medical College and Bailey Thoracic Clinic, Philadelphia. The superior and inferior venae cavae of anaesthetized dogs were cannulated, and a ligature round each cannula enabled the entire systemic circulation to be shunted around the right heart. The blood was reintroduced into the distal pulmonary artery beyond another ligature. Thus the only inflow into the right heart was from the coronary circulation, and represented the entire coronary venous drainage with the exception of that which is supposed to return to the left heart. A cannula in the proximal portion of the pulmonary artery drained the outflow from the right ventricle into a graduated flask, permitting measurement of the coronary flow. This blood was reintroduced into the external side of the circulation (pulmonary artery). By means of this procedure the systemic flow was compared with the coronary flow, and the oxygen consumption of the heart itself was accurately measured.

After administration of noradrenaline and adrenaline the increase in coronary circulation (and oxygen supply) was greater than the increase in oxygen utilization by the heart. Further, when the coronary blood flow was increased 15 times the systemic blood flow through the rest of the body remained at the same level. Thus the beneficial effect of noradrenaline in myocardial infarction is probably due to the increase in coronary blood flow, which is much greater proportionately than the rise in blood pressure.

[These results were obtained in dogs, in which noradrenaline is a potent coronary vasodilator; the drug does not have the same effect in all species.]

G. B. West

678. **Tiphen and Promedol in the Treatment of Coronary Disease.** (Применение тифен-промедола при коронарной болезни)
A. I. Gefter and A. P. Matusova. *Советская Медицина* [*Sovetsk. Med.*] 22–25, No. 8, Aug., 1955.

Coronary arterial disease has been treated at the Kirov Medical Institute with a combination of " tiphen " (hydrochloride of di-ethylaminoethyl ester of thiodiphenyl acetic acid) and " promedol " (1:2:5-trimethyl-4-phenyl-4-propion oxypiperidine hydrochloride), both of which are effective in this condition. A total of 36 patients (31 men and 5 women) were under observation, all having well-marked stenocardia and, in 29 cases, electrocardiographic (ECG) evidence of cardiac disease; 17 were diagnosed as having acute myocardial infarction. Tablets containing 30 mg. of tiphen and 25 mg. of promedol were given to 27 of the patients three times daily for 8 to 14 days; the other 9 patients received the tablets only if pain occurred.

In acute infarction the tablets did not at first abolish pain, proving more effective in cases of dull, aching, retrosternal pain or in severe spasms of angina, though in this last condition they were slower in action than nitroglycerin. The results of combined treatment with the two drugs were superior to those achieved with either drug alone. The final results were " good " in 9 cases (abolition of pain, as also of cutaneous paraesthesiae, and improvement in the ECG pattern), " satisfactory " in 14 (relief of symptoms without complete remission of vascular and ECG disturbances), and " poor " in 4.

[Promedol is similar to pethidine in its composition; tiphen appears to have some affinity with aminophylline, and resembles papaverine in its pharmacological effect.]

L. Firman-Edwards

HYPERTENSION

679. **Drug Therapy in Hypertension with Hemorrhagic Hypertensive Retinitis**
C. F. Burnett and J. A. Evans. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 395–398, Sept. 8, 1955. 3 figs., 2 refs.

In this paper from the Lahey Clinic, Boston, experience of the use of ganglion-blocking agents in the treatment of 56 patients with Grade-3 and 22 with Grade-4 hypertensive retinitis is reported. Because of easier control pentolinium is preferred to hexamethonium, but before either drug is given all patients receive a course of reserpine or a preparation of *Rauwolfia serpentina* lasting 3 to 6 weeks. Hydrallazine (" apresoline ") has been abandoned for this " priming " course (which is thought to reduce the amount of ganglionic-blocking agent required and lessen side-effects) because of its toxicity.

To begin with, pentolinium was given by mouth in a dosage of 10 mg. four times a day (before meals and at

bedtime), the dosage being then adjusted to keep the diastolic pressure, with the patient standing, between 90 and 110 mm. Hg. A "significant" fall in blood pressure occurred in 53 of the Grade-3 and 16 of the Grade-4 cases. [No details are given other than the numbers of patients thought to be improved, unchanged, and worse and the number surviving over unstated periods.] *P. Hugh-Jones*

680. **Hemodynamic Changes in the Bulbar Conjunctival Capillary Bed of Subjects with Hypertension Associated with "Cushing's Syndrome" or Pheochromocytoma**
R. E. LEE. *American Journal of Medicine* [*Amer. J. Med.*] 19, 203–208, Aug., 1955. 4 figs., 3 refs.

Patients with hypertensive vascular disease have been shown to display certain changes in the capillary bed of the bulbar conjunctiva. Briefly, these consist in vasoconstriction of the minute terminal arterioles, increased reactivity of these vessels to topically applied adrenaline, reduction in the velocity of the peripheral blood flow, and elongation, coiling, and tortuosity of the true capillaries. These features may be seen individually in normal subjects, but occur in association only in hypertension.

The conjunctival capillary bed was examined at the Cornell University–New York Hospital Medical Center in 5 cases of Cushing's syndrome and 3 of large functioning phaeochromocytoma, in all of which hypertension was present. No difference was observed between the changes found in Cushing's disease and those of essential hypertension. In the cases of phaeochromocytoma, however, although some degree of vasoconstriction was present, there was a complete absence of capillary coiling, tortuosity, and elongation, and diminished hyperreactivity of the arterioles and precapillaries to topically applied adrenaline; a distinctive feature was the variation in degree of the vascular changes present with changes in blood pressure in contrast to their stability in essential hypertension. The possible physiological importance of these findings is discussed. *Francis Page*

681. **Results of Splanchnicectomy on Patients with Hemorrhagic Hypertensive Retinitis**
I. HUNTINGTON and J. A. EVANS. *New England Journal of Medicine* [*New Engl. J. Med.*] 253, 398–403, Sept. 8, 1955. 2 figs., 12 refs.

The results of splanchnicectomy in 206 patients with Grade-3 or Grade-4 haemorrhagic hypertensive retinitis at the time of operation are reported in this paper from the Lahey Clinic, Boston. Of the 206 patients, 189 were followed up for 4 to 19 years, and the survival rate in this group is compared with that reported by others for similar groups treated medically before the advent of the new hypotensive drugs. In patients with Grade-3 retinopathy the cumulative survival rate was 46% in 10½ years, compared with an expected survival rate of *nil* as reported by Keith *et al.* (*Amer. J. med. Sci.*, 1939, 197, 332). In patients with Grade-4 retinopathy the "relative survival rate" (the observed survival rate contrasted with that expected for a life-table population) was compared with that in a group studied by Palmer and Muench (*J. Amer. med. Ass.*, 1953, 153, 1; *Abstracts of World Medicine*, 1954, 15, 229) in which medical treatment without hypotensive drugs was given. The relative survival rate in the present series was 39·9% in 6½ years, as against an expected rate of 5·6%. From these figures the authors conclude that in spite of the advent of the new hypotensive drugs, there is a place for splanchnicectomy in young hypertensive patients with haemorrhagic retinitis [in whom the prognosis is so grave without treatment], provided renal function is still good.
P. Hugh-Jones

682. **The Treatment of Hypertension by the Rectal Infusion of a Mixture of Hypnotic Drugs.** (Лечение гипертонической болезни путем ректального введения комбинированной смеси)
Z. L. LILEEVA. *Терапевтический Архив* [*Ter. Arkh.*] 27, 64–67, No. 5, 1955. 12 refs.

The author describes the treatment of 21 patients suffering from hypertension by the rectal infusion of a solution of various hypnotic drugs. Nearly all the patients complained of headaches, giddiness, noises in the ears, pains in the extremities, insomnia, and general weakness. In 10 cases the blood pressure reached 200/120 mm. Hg and in the remaining 11 it was 170/100 mm. Hg. It is claimed that 18 of the 21 patients benefited.

The mixture used for the enema consisted of 20 to 30 ml. of alcohol [strength not given], 0·2 g. of "nembutal" (pentobarbitone sodium), 1 g. of magnesium sulphate, and 1 g. of sodium bromide dissolved in 100 ml. of water. This solution was administered per rectum twice a day and always by the same nurse, once in the morning after breakfast and again before retiring to sleep. Constipated patients were given first a purgative enema. The patients generally went to sleep 5 to 10 minutes after the administration of the enema and slept for up to 4 hours. After about 3 days a conditioned reflex was established and the patients went to sleep even when the enema consisted only of water, provided it was administered by the same nurse and at the same time. However, this conditioned reflex leading to sleep became weaker after 4 to 8 days and the solution of drugs had to be given again for a while.

It was noted that the blood pressure always fell following administration of the drug-containing enema, but that the reduction in pressure was small following the conditioned reflex sleep. *A. Orley*

683. **Depression and Anxiety Occurring during Rauwolfia Therapy**
J. C. MULLER, W. W. PRYOR, J. E. GIBBONS, and E. S. ORGAIN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] 159, 836-839, Oct. 29, 1955. 12 refs.

684. **The Significance of the Pitot Pressure in the Intra-arterial Measurement of Blood Pressure in Man.** (Über die Bedeutung des Pitotdruckes für die intra-arterielle Blutdruckmessung beim Menschen)
K. CYVIN, J. JÖRSTAD, and N. RETTERSTÖL. *Acta medica Scandinavica* [*Acta med. scand.*] 152, 491-497, 1955. 4 figs., 10 refs.

Haematology

685. **Studies in Sickle-cell Anemia. V. Sickle-cell Hemoglobin C Disease**
R. B. SCOTT and M. E. JENKINS. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **90**, 35–42, July, 1955. 3 figs., 25 refs.

The two abnormal varieties of haemoglobin encountered most frequently in American negroes are haemoglobin S and haemoglobin C. Whereas the combination in an individual of the gene for normal adult haemoglobin (A) with that for haemoglobin S or with that for haemoglobin C is considered to be harmless, the heterozygous combination of the S and C genes gives rise to a modified form of sickle-cell anaemia, sickle-cell–haemoglobin-C disease, which has a fairly characteristic clinical appearance. The authors, writing from Howard University College of Medicine and Freedmen's Hospital, Washington, D.C., remark on the dearth of descriptions of this condition in the paediatric literature. In order to make this particular variety of sickle-cell disease more widely known they here describe 2 cases of the condition occurring in siblings. The paper includes a valuable review of the current literature on the subject, photomicrographs of target cells and sickling cells, illustrations of the electrophoretic patterns of the various abnormal haemoglobins, and a summary of the findings in the 19 cases previously reported.

H. Lehmann

686. **Liver Disease in Sickle Cell Anemia. A Correlation of Clinical, Biochemical, Histologic and Histochemical Observations**
A. BOGOCH, W. G. B. CASSELMAN, M. P. MARGOLIES, and H. L. BOCKUS. *American Journal of Medicine* [*Amer. J. Med.*] **19**, 583-609, Oct., 1955. 9 figs., bibliography.

687. **Megaloblastic Anemia Associated with Anatomic Lesions in the Small Intestine**
R. B. THOMPSON and C. C. UNGLEY. *Blood* [*Blood*] **10**, 771–787, Aug., 1955. 5 figs., 20 refs.

It has been known for many years that an anaemia resembling Addisonian pernicious anaemia may result from lesions in the small intestine. In this paper from the Royal Victoria Infirmary, Newcastle upon Tyne, 6 cases are described in which intestinal strictures or anastomoses were associated with macrocytic anaemia. In 3 cases a megaloblastic change was diagnosed on the basis of clinical and laboratory findings and because there was some degree of improvement following administration of liver extract; in the other 3 (more recent) cases erythropoiesis was shown to be megaloblastic. There was concomitant iron deficiency in some of the cases and in one case initially there was pure iron-deficiency anaemia. The responses to crude and refined liver extracts and to cyanocobalamin were poorer than those expected in Addisonian pernicious anaemia; they were comparable to the responses observed in megaloblastic anaemia associated with idiopathic steatorrhoea. Slight atrophy of the lingual papillae was noted in 3 cases and another patient had ulceration of the tongue and gums. There was no evidence of neurological involvement. The bulky, offensive stools characteristic of idiopathic steatorrhoea were seen in only one case; in 4 cases steatorrhoea was inconstant; in the last case diarrhoea was not present. Only 2 patients had histamine-fast achlorhydria.

The intestinal lesions were: (1) stricture of the ileum at the site of an adherent appendix; (2) one stricture of the lower ileum due to sloughing of a segment of bowel following intussusception in childhood, and two others due probably to tuberculous ulceration; (3) acute and chronic jejunal ulceration, with stricture; (4) massive ileal resection and ileo-transverse colostomy for regional ileitis; (5) ileocolic fistula, detected 28 years after tuberculous peritonitis; (6) ileostomy following multiple operations on the small bowel for traumatic rupture. Operations undertaken to by-pass strictures did not relieve the anaemia so long as stagnant loops of bowel remained.

Discussing the relationship of the intestinal lesion to the development of megaloblastic anaemia, the authors suggest that the small intestine is invaded by colonic organisms which may interfere with the normal bacterial inhabitants and hence with the biosynthesis of haematopoietic factors, or they may absorb such factors as nutrients for their own growth; another possibility is that the organism may elaborate substances which inhibit erythropoiesis but which are detoxified by cyanocobalamin or folic acid, so long as supplies of these last. Increased demands for cyanocobalamin may play a part in the production of the megaloblastic anaemia.

T. B. Begg

LEUKAEMIA

688. **Preliminary Observations on the Action of Yeasts in Leukaemia.** (Prime osservazioni sull'azione dei lieviti nelle leucemie)
G. PROTTI. *Tumori* [*Tumori*] **41**, 273–288, May–June, 1955 [received Sept., 1955]. 9 figs., 18 refs.

Investigations carried out at the Oncological Centre, Ancona, Italy, have shown that leukaemic leucocytes undergo degenerative changes, agglutination, and finally lysis when exposed *in vitro* to the action of certain yeasts, whereas normal leucocytes are unaffected.

Various yeasts were injected intravenously into 5 patients suffering from acute leukaemia, 1 from subacute leukaemia, 1 from chronic myeloid leukaemia, and 2 from chronic lymphatic leukaemia. No haematological or clinical improvement resulted in the patients with acute or subacute leukaemia. In the patient with chronic

myeloid leukaemia, however, after the intravenous injection of *Rhodotorula rubra* (selected by tests *in vitro* on the patient's leucocytes) the leucocyte count fell from 260,000 to 80,000 per c.mm. in about 4 months, but the patient died after 5 months. One of the patients with chronic lymphatic leukaemia was treated with the same organism (without previous testing *in vitro*), the leucocyte count falling from 20,000 to 8,000 per c.mm. in 3 weeks, while the other was treated with *Cryptococcus albidus* (selected by testing *in vitro*), the leucocyte count falling from 70,000 to 20,000 per c.mm. in 10 days. Both these patients showed marked clinical improvement, which was still being maintained at least 7 months after treatment started. *M. Lubran*

689. **The Treatment of Acute Leukaemia**

R. Bodley Scott. *British Medical Journal* [*Brit. med. J.*] 2, 75–77, July 9, 1955. 1 fig., 21 refs.

The author briefly reviews the methods now available for the treatment of acute leukaemia, with reference to the recent literature, and reports the results obtained in 121 of his own cases. Of 46 cases treated with transfusion alone, significant remissions were seen in 9. Exsanguination transfusion was carried out in 3 cases, but the results were not good and in the author's opinion this method should be abandoned. Folic acid antagonists were used in a small number of cases but the results were not very promising. 6-Mercaptopurine was tried in 10 cases; a good remission resulted in one child and one adult and a moderate remission in another child, but the drug had little effect on 5 of the remaining patients and none at all on 2 with monocytic leukaemia. Cortisone or corticotrophin was used in 23 cases, resulting in 7 complete and 4 partial remissions; again monocytic leukaemia was unaffected.

The author considers that transfusions should be used to maintain the haemoglobin level at about 50 to 60% and that antibiotics should be used for the treatment of specific infections, but not as a "cover". He points out the difficulties of dealing with the haemorrhagic states complicating acute leukaemia.

In his experience remission is most probable in children under 12, especially in cases of "the lymphoblastic variety, particularly of the purely medullary type". The effect of any specific treatment in prolonging life is difficult to assess because of the wide natural variations in the duration of acute leukaemia.

It is recommended that 6-mercaptopurine, which has negligible toxic effects, should be tried first in cases of acute leukaemia in adults. This can be combined with or followed by treatment with cortisone, which should also be given in cases of the lymphoblastic and myeloblastic types that are not responding to mercaptopurine or blood transfusion. Folic acid antagonists "have no place in the treatment of acute leukaemia in adults". In children with rapidly advancing disease cortisone or corticotrophin should be used initially, antimetabolites being reserved for the first signs of relapse. In less acute cases in children, however, antimetabolites should be given preference, changing from one to another as resistance develops. "Specific" drugs should not be given during remission. *M. C. G. Israëls*

690. **The Influence of Chemotherapy on Survival in Acute Leukemia**

A. Haut, S. J. Altman, G. E. Cartwright, and M. M. Wintrobe. *Blood* [*Blood*] 10, 875–895, Sept., 1955. 6 figs., bibliography.

In order to assess the life-prolonging effect of various agents used in the treatment of acute leukaemia, data from the records of 103 cases treated at the clinic of the University of Utah College of Medicine, Salt Lake City, between March, 1947, and March, 1954, which subsequently proved fatal, were studied. The records of 33 other cases seen during this period were insufficiently complete to allow of their inclusion, while 8 others received specific treatment over an inadequate period and were similarly excluded. Of the 103 cases, 57 were of lymphoblastic, 42 of myeloblastic, and 3 of monoblastic leukaemia. The sex distribution was approximately equal; 50 of the patients were aged under 11 and 40 over 20. The period of survival in each case was estimated in months from the onset of the first symptom attributable to leukaemia or which led to the diagnosis of leukaemia, and varied from one to 20 months. For each group studied the duration of the disease was plotted on log-probability paper against the proportion surviving at the corresponding monthly intervals, and the times at which 50% and 10% of the group remained alive estimated to the nearest half-month. The results were subjected to the usual procedures of statistical analysis.

The patients fell into three groups: (1) 11 patients received no specific treatment (treatment with blood transfusion and antibiotics being regarded as non-specific); (2) 10 received "non-standard" treatment, the agents used including x rays, nitrogen mustard, urethane, "myleran", and radioactive phosphorus; and (3) 82 patients received "newer therapies"—that is, folic acid antagonists, ACTH (corticotrophin) and cortisone, and 6-mercaptopurine, used singly, successively, or in various combinations. To the results in this series were added those obtained in 782 cases recorded in the literature from which adequate data were available and which had been treated since the introduction of antibiotics. Of these, 143 received no specific treatment, 434 "non-standard" treatment, and 205 the "newer therapies".

For the authors' Group 1 (11 cases) the 50% survival time was 2 months and the 10% survival time 8 months. The survival figures for the corresponding group from the literature (143 cases) were 4½ and 11 months respectively. For Groups 1 and 2 combined (21 cases) the 50% and 10% survival times in the authors' series were 3 and 11 months, and in the additional series (577 cases) 4 and 9½ months respectively. For Group 3 the 50% and 10% survival times in the authors' series (78 cases) were 5½ and 11 months, and in the series from the literature (205 cases) 5 and 11¼ months respectively.

There was no statistically significant difference between any of these results, nor was there any difference between the survival times of children and adults in Group 3. The authors therefore conclude that the treatment of acute leukaemia with the "newer therapies" in a random group of cases does not appear to prolong life

significantly. In 26 of their own cases, however, temporary complete remissions were obtained with such treatment, and the 50% and 10% survival times were 8 and 14 months respectively. They suggest that there are three possible explanations of this apparent discrepancy: (*a*) that the drugs actually shortened life in some cases and prolonged it in others; (*b*) that the number of cases in which this treatment was given was inadequate for statistical purposes; and (*c*) that the drugs (especially 6-mercaptopurine) were not always being used in the most efficient way.

[No mention is made of the dosage of the therapeutic agents used, nor is the effect of treatment studied in relation to the different types of acute leukaemia. In the authors' Group 3 a variety of agents were used in a variety of different combinations and, as they point out, the numbers treated with each individual drug or combination of drugs were too small to allow of separate analysis.] *M. Kendal*

BLOOD TRANSFUSION

691. **The Preservation of Blood for Transfusion. I. The Effect of Plastic Containers on Red Cells**

M. M. STRUMIA, L. S. COLWELL, and K. ELLENBERGER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 225–233, Aug., 1955. 3 figs., 18 refs.

The effect on stored blood of the use of plastic containers was studied in comparison with blood taken into the same anticoagulent but stored in boro-silicate containers. The investigations included the estimation of post-transfusion erythrocyte survival *in vivo* and haematological and biochemical studies *in vitro*.

The results varied considerably with different plastic containers, even from the same manufacturer, some containers appearing to have a deleterious effect on the stored blood, as shown by a reduction in erythrocyte survival, while others appeared to enhance erythrocyte survival. The plastic used for all the containers tested was basically polyvinyl chloride, the production of which is not standardized, variable factors such as the plasticizers, stabilizers, and mould inhibitors used in manufacture, and even the detergents used for washing the material, being likely to affect the finished product and hence the blood stored therein. Therefore the authors are of the opinion that plastic containers cannot be recommended for general use until rigid standardization in manufacture is possible. *I. Dunsford*

692. ***In vitro* Comparison of the Effects of Four Different Preservative Solutions on Single Donor Blood, with Special Emphasis on Rate of Flow**

H. CHAPLIN and E. CHANG. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 234–244, Aug., 1955. 3 figs., 8 refs.

Several acid–citrate–dextrose solutions are in common use as anticoagulants for donor blood, all differing slightly in the proportions of the constituents and the volumes to be added per unit volume of blood. Of these, 4 were selected for a comparative study of their effect on the blood during storage, with particular reference to the rate of flow of the blood on administration, at the National Microbiological Institute, Bethesda, Maryland.

Three healthy donors were bled by the gravity method, the blood being received into each of the 4 different anticoagulants in turn to give 4 100-ml. volumes of citrated blood from each donor. During the withdrawal of the blood thorough mixing with the anticoagulant was secured and on completion each bottle was inverted 4 or 5 times. Before use for transfusion each bottle was sharply inverted 10 to 12 times.

The rate of flow during transfusion depends upon the difference between the transfusion pressure and the opposing venous pressure, the length and diameter of the narrowest part of the apparatus used (usually the needle), the proportion of erythrocytes present in the blood, and the nature of the suspending fluid. Allowing for these factors it was found that the differences between the effects of the mixtures studied or the rate of flow were negligible. Furthermore, observations on cell volume, plasma haemoglobin content, and erythrocyte fragility revealed no important differences between the four anticoagulants.

Emphasis is placed on the necessity for adequate mixing during taking and before transfusion to facilitate the administration of blood. *I. Dunsford*

693. **Citric Acid Intoxication**

J. P. BUNKER, J. B. STETSON, R. C. COE, H. C. GRILLO, and A. J. MURPHY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 1361–1367, April 16, 1955. 2 figs., 18 refs.

During extremely rapid and prolonged transfusion of citrated blood, citric acid intoxication may occur. At Massachusetts General Hospital, Boston, the serum concentrations of citrate, calcium, magnesium, potassium, and total proteins were estimated in 130 patients during transfusion of moderate or large volumes of citrated whole blood. Each unit of transfused blood contained 75 ml. to 125 ml. of a solution containing 1·33% of sodium citrate, 0·47% citric acid, and 3% dextrose. If the transfusion rate remained below 0·5 mg. of citrate per kg. body weight per minute, the serum concentration of citrate ion and the ionized calcium level remained within normal limits. Only patients with advanced liver disease showed poor citrate tolerance. However, when the transfusion rate was increased to 1 mg. of citrate per kg. per minute the serum citrate concentration rose in half of the patients with normal liver function to above 9 mg. per 100 ml., while the ionized calcium level showed a tendency to fall. There was no correlation between increase in coagulation time and depression of the ionized calcium level. Tetany was not observed. Calcium salts administered intravenously were found not to be very satisfactory in the treatment of patients with citric acid intoxication. It is suggested that in patients with impaired liver function decalcified blood or resuspended erythrocytes should be used for rapid and prolonged transfusions.

Kate Maunsell

Respiratory System

694. **Respiratory Function following Pulmonary Infarcts**
O. JACOBY, T. SØNDERGAARD, and H. H. WANDALL. *Thorax* [*Thorax*] **10**, 127–130, June, 1955. 10 refs.

Bronchospirometric measurements were carried out at varying periods of time after fairly large pulmonary infarcts in five patients. In addition, one of these patients was examined by angiocardiopulmography. The observations show that, with disappearance of consolidation on the *x*-ray film, the ventilation capacity is normal, while the oxygen uptake need not reach normal values.—[Authors' summary.]

695. **Intralobar Sequestration of the Lung**
R. A. SMITH. *Thorax* [*Thorax*] **10**, 142–152, June, 1955. 9 figs., 25 refs.

The anomaly known as intralobar sequestration of the lung consists of an ectopic mass of lung, situated usually within the lower lobe in the vicinity of the pulmonary ligament, and supplied by an aberrant artery in the region of the diaphragm. It occurs rather more frequently on the left side (57% of 47 cases reported in the literature), but may be bilateral. The artery is large and elastic, in the latter respect resembling a pulmonary artery. The venous drainage is usually to the pulmonary vein. The bronchi of the ectopic mass may be dilated or even grossly cystic. Infection is common and as a result there is generally a secondary communication with the bronchial tree.

The present paper from the King Edward VII Hospital, Warwick, describes 4 cases. Much useful information is marshalled, new observations made, and the theories of origin critically examined. *D. M. Pryce*

696. **Chronic Bronchitis. The Effect of Cigarette-smoking**
N. C. OSWALD and V. C. MEDVEI. *Lancet* [*Lancet*] **2**, 843–844, Oct. 22, 1955. 2 refs.

To assess the significance of cigarette smoking in the aetiology of chronic bronchitis, the authors studied the incidence of this condition in 3,587 smokers (5 or more cigarettes a day for at least 5 years) and 2,257 non-smokers (including pipe-smokers) drawn from Civil Service clerical staff. Trained welfare workers, under the supervision of one of the authors at the Brompton Hospital, London, obtained detailed histories from the subjects in both groups. Neither physical nor radiological examination was carried out, but the authors consider that any possible error introduced by this omission was not significant. Cough and sputum only were not regarded as adequate indices of chronic bronchitis, reliance in diagnosis being placed on breathlessness and "exacerbations of infection of sufficient severity to interfere with the normal mode of life".

Of the smokers, 36% were free from respiratory symptoms, 48% had mild symptoms, and 15·9% had bronchitis; the corresponding figures in non-smokers were 53%, 38%, and 9·4%. [In neither group do the figures total exactly 100%.] Over the whole series the incidence of bronchitis was 13·4% and appeared to rise with age, but was strikingly similar in males and females.

The authors cautiously conclude that "the proportion of clerical workers having minor respiratory symptoms and bronchitis was consistently higher in smokers than in non-smokers". *F. Starer*

697. **The Long-term Clinical and Functional Results of the Operative Treatment of Bronchiectasis.** (Über klinische und funktionelle Spätresultate operativ behandelter Bronchiektasien)
E. STRAHBERGER and M. WENZL. *Thoraxchirurgie* [*Thoraxchirurgie*] **3**, 160–166, Aug., 1955. 11 refs.

Ten years ago the opinion was generally held that the outlook in bronchiectasis treated conservatively was bad, many patients dying of severe complications or being completely incapacitated by the disease. Perry and King reported in 1940 a mortality of 26% over a period of 12 years, nearly one-half of these deaths occurring within the first 5 years; this was, of course, before the introduction of antibiotics. The use of these agents has undoubtedly produced a great improvement in the general condition of bronchiectatic patients, but it is not yet possible to estimate whether such treatment has produced a favourable effect on the prolongation of life. The preoperative administration of antibiotics has reduced the operative mortality from 30 to 2%.

The present inquiry was made at the University Second Surgical Clinic, Vienna, 54 cases of bronchiectasis treated there between 1947 and 1951 being reviewed. In 13 cases treatment was conservative, and 7 of these patients have died either of the disease or its complications. The average duration of the disease in these 7 was 16 years, while in the 6 still alive it has been 18 years. Since in those who died the process was generally diffuse and bilateral, while in those who have survived it has remained localized, it would appear that the extent of the disease process is the decisive factor determining the duration of life. Only one patient, in spite of bilateral bronchiectasis, was free from any clinical or functional disorder.

In 6 cases palliative measures only were undertaken; 3 patients subjected to pneumotomy died shortly after the operation, 2 underwent thoracotomy, and one patient operated on by Graham's method has, after 3 years, very little complaint. The remaining 34 cases were treated surgically at various times 4 to 8 years previously; in 21 the process was limited to one lobe, this being the lower in 16 cases. Of the 34 cases, 27 (79%) were found to be cured or improved and 7 (21%) had not benefited —figures which agree with those reported in the literature by other workers. Bronchographic examination showed that bronchiectasis was present in the remaining lung

tissue in 8 cases, but it was difficult to be certain whether this was a new formation or residual. Although incomplete resection of diffuse bronchiectasis brought some temporary improvement, the long-term results were especially bad, while local bronchiectasis remaining after resection also gave a bad result.

Determination of pulmonary functional efficiency after operation showed that this was complete in 11 cases, good in 16, reduced in 3, and bad in 4. Respiratory capacity in 79% of cases approximated to the normal, but the other 21% showed a marked reduction. The authors state that apart from the cure of the basic disease, the eventual functional result depends upon the ability to compensate for loss of lung parenchyma. After resection of only one lobe no perceptible deviation from the estimated ventilation capacity could be established. On the other hand, after more extensive resection, alterations occur which indicate an expansion of the remaining parenchyma. The condition of the remaining parenchyma depends also on the patient's age; a table is presented which shows that up to the age of 50 no pathological change can be established, but after that age there is an increasing tendency towards emphysema. *D. P. McDonald*

698. **Resectable Bronchogenic Carcinoma. A Study of 120 Cases**

G. H. ALVAREZ. *Diseases of the Chest* [*Dis. Chest*] **28**, 217–227, Aug., 1955. 8 figs., 6 refs.

The clinical features in 120 cases of bronchogenic carcinoma successfully treated by lung resection were studied at the Hospital Nacional de Clínicas, Buenos Aires, with the object of determining the symptomatology, if any, of early and resectable tumours. Significant early signs and symptoms were haemoptysis in 34 cases, bronchoscopic evidence of growth in 37, and rheumatoid conditions, including the Bamberger–Marie syndrome, in 22. The author states that the latter syndrome in association with a shadow in the lung radiograph is almost pathognomonic, and is frequently encountered where there are small peripheral growths, which are commonly adenocarcinomata of relatively low malignancy; in 17 of the 22 cases in this series the tumour was an adenocarcinoma. *S. F. Stephenson*

699. **Natural Duration of Bronchial Carcinoma**

J. R. BIGNALL. *Lancet* [*Lancet*] **2**, 210–214, July 30, 1955. 2 figs., 13 refs.

During 1951 and 1952 at the Brompton and Royal Marsden Hospitals, London, 637 cases of bronchial carcinoma were seen, 135 being treated surgically, 210 by irradiation, and 292 receiving no treatment "likely materially to prolong life". This last untreated group provided the author with an opportunity to study the natural duration of the disease, because in 255 of them the time at which symptoms first occurred was known. However, 14% of the patients in this group were alive 2 years or more after the first symptom was noted, and the pattern of survival is therefore expressed as the "median duration—the time by which half the patients were dead". The median duration for the whole group of untreated patients was 9 months. It was longer (11½ months) in 84 cases of "differentiated" carcinoma, and shorter (7½ months) in 45 cases of "undifferentiated" tumours. The median survival time was similar in cases with and without metastases. It was found that the duration of illness was not affected by age, sex, or the lobe in which the tumour was situated. Prognosis, however, was greatly influenced by the duration of symptoms before diagnosis; when symptoms had been present for only 4 to 5 months half the patients were dead within the following 3 months, but when symptoms had been present for 12 months half of the patients lived a further 7 months. *D. M. Pryce*

700. **The Use of Prednisone ("Meticorten") in Respiratory Disease. II. Pulmonary Emphysema and Pulmonary Fibrosis**

H. A. BICKERMAN, G. J. BECK, and A. L. BARACH. *Journal of Chronic Diseases* [*J. chron. Dis.*] **2**, 247–259, Sept., 1955. 8 figs., 11 refs.

Prednisone ("meticorten") was given in the treatment of 50 patients with pulmonary emphysema and fibrosis at the Presbyterian and Goldwater Memorial Hospitals, New York. If bronchospasm was marked the dosage was 60 to 80 mg. a day for the first day or two; thereafter it was reduced by 10 to 20 mg. each 2 or 3 days; at the end of 7 to 10 days a maintenance dose of 10 to 25 mg. was usual. If bronchospasm was moderate the initial daily dose was 40 to 50 mg. The drug was given with milk at mealtimes and between 11 and 12 p.m., and aluminium hydroxide or calcium carbonate was given 2 hours after main meals and on retiring. No dietary limitations were imposed except for salt restriction in cases of obvious heart failure. Most patients showed considerable improvement within 48 hours; only 7 had no relief. In 15 patients vital capacity increased, on the average, by 32%, the increase being most marked in those in whom bronchospasm was a prominent feature. Improvement was also noted in the maximum breathing capacity and in the resting minute ventilation breathing air and 100% oxygen. Loss of weight was observed in 12 patients during prednisone therapy. There was no change in the serum biochemistry, but after two months of treatment one patient showed a reduction in urinary excretion of 17-ketosteroids. Adverse side-effects included transitory headache, increased nervous tension, slight "moon-face", and, more particularly, reactivation of pulmonary or sinus infection, thrombophlebitis of the leg, and gastro-intestinal discomfort with exacerbation of peptic ulceration, this last, in the authors' view, being diminished by giving prednisone in milk with an antacid. It is suggested that weight loss, in the absence of overt heart failure, may be due to fluid loss from inflamed lung tissue. If there was fluid retention due to previous cortisone therapy or to heart failure, prednisone produced a diuresis which the authors ascribe partly to the relief of hypoxia. Among the advantages of prednisone compared with cortisone are the more constant response, the lower dosage, and the absence of fluid retention even when the diet is normal. *L. Capper*

Otorhinolaryngology

701. **Auditory Fatigue and Adaptation in the Differential Diagnosis of End-organ Disease**
J. D. HOOD. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol. (St Louis)*] **64**, 507–518, June, 1955. 6 figs., 7 refs.

It has been shown that if a sustained noise is applied to one ear the sensation of loudness rapidly diminishes, and that in order to match the intensity of the sound by applying a noise of apparent equal loudness to the other ear a much smaller intensity is required after 3 minutes than is needed at the beginning of the experiment. This phenomenon is thought to be due to adaptation. If the same test is applied to an ear affected by Ménière's disease the sensation of loudness is lost more quickly than it is in a healthy ear. In both cases the sensation of loudness returns to its previous strength after a short interval; the alteration is therefore not due to fatigue, from which the period of recovery is far longer.

In this paper from the National Hospital, Queen Square, London, the author describes how this quality of rapid adaptation in Ménière's disease may be studied by the use of two audiometers; in the first test the sound is presented to the subject at its full strength, while in the second the sound is gradually increased to its maximum over an interval. In the first case, if Ménière's disease is present, adaptation does not occur and the audiograph shows a smaller loss than in the second test in which adaptation occurs while the sound is reaching its maximum. In middle-ear deafness, on the other hand, the audiographs obtained by the two methods are alike, for in this type of deafness adaptation takes place as in a normal subject. It is suggested that in Ménière's disease the increase in adaptation to the test tones of the audiometer is due to a change in the cochlea.

William McKenzie

702. **Stapes Mobilization in Otosclerosis. Primary Results and a Review of Sixty-three Cases**
Y. MEURMAN and O. MEURMAN. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **62**, 164–172, Aug., 1955. 2 figs., 17 refs.

In this paper from the University of Helsinki the authors discuss particularly the theoretical possibilities of Rosen's revival of the Miot method of mobilization of the stapes in otosclerosis. The usual site of the otosclerotic focus is in front of the oval window, and as it seems that a very small free area of the round window is adequate for transmission of vibrations, for practical purposes the disability consists in fixation of the stapes in the oval window, usually with extension of a focus from the anterior margin growing through the annular ligament into the footpiece. The extent of the growth and the degree of fixation are very variable. If the bony connexion between the stapes and the window margin is stronger than the crura of the stapes, it will not be possible to mobilize it. The degree of fixation does not seem to be related to duration of the condition. Of 11 cases in which hearing was improved by the operation, movement of the stapes caused vibration of the membrane of the round window in 10, whereas this occurred in only one out of 8 cases in which there was no improvement. The proportion of the authors' 63 cases in which improvement was obtained was not quite so high as after fenestration. On the other hand in some cases the result was better than would normally have been expected after fenestration. The principal cause of failure was fracture of the crura, and the principal accidents were luxation of the incudo-stapedial joint, rupture of the membrana tensa, and (in 2 cases) transient facial palsy.

F. W. Watkyn-Thomas

703. **Mobilization of Middle-ear Structures through the Eustachian Tube**
S. DALY, L. J. GOLDSTEIN, M. HELLER, B. ANDERMAN, and M. M. EZEKIEL. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **62**, 187–197, Aug., 1955. 10 figs., 16 refs.

The authors claim that in a variety of types of deafness improvement can be obtained by mobilizing the structures of the middle ear by means of a flexible bougie passed through the Eustachian tube, a method introduced in 1724 by Guyot but generally discarded. The operator manipulates the nylon bougie while an assistant watches the tympanic membrane through an otoscope, movement of the membrane indicating that the attempt to mobilize has been successful, though this does not necessarily mean improvement of hearing. This method has been used in the treatment of adhesive conditions following healed suppuration and in some cases in the presence of active suppuration [numbers not specified].

It is stated that " preliminary investigations seem to show that this method has apparent limited benefit even in long-standing cases of clinical otosclerosis where slight mobility of the drum membrane and ossicles persists and can be activated ". No attempt is made to give " any exact explanation of the mechanism of the bougie pressure on middle-ear structures ".

F. W. Watkyn-Thomas

704. **Acoustic Trauma**
M. SALTZMAN and M. S. ERSNER. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **62**, 235–241, Sept., 1955. 4 figs., 15 refs.

The authors, writing from Temple University School of Medicine, Philadelphia, distinguish three different types of acoustic trauma. (1) The insidious and slowly progressing type found in persons who have been exposed to noise for years, most of whom have some degree of hearing deterioration. Prophylaxis consists in making the working conditions quieter and using ear protectors. (2) The " sound-injured " inner ear, which often follows a brief exposure to gun-fire, is characterized by a wedge-

shaped high-tone loss which is " precisely measurable ", tinnitus, diplacusis, and marked lowering of the threshold of discomfort. Treatment includes the provision of quiet working conditions, raising the threshold of discomfort by using ear protectors, and, in some cases of tinnitus, exposure for a long time to specific sounds to mask the tinnitus and increase the patient's tolerance to " sounds in the ear " [a very interesting suggestion]. (3) Progressive degeneration after sound injury. In some cases deterioration continues without any further exposure to noise, leading to premature presbyacusis. The patient must be protected against further exposure, infection, avitaminosis, and drugs toxic to the cochlea.

The authors discuss experimental work on acoustic trauma and suggest that the lack of hearing loss after brief exposure to noise from a jet engine in contrast to the loss which occurs on exposure to noise from a piston engine is due to the fact that the ear adapts better to noise free of sudden peaks of intensity and with mixed frequency components. They also draw attention to Cantor's hypothesis that sound waves of high intensity may reach the middle ear through the patent Eustachian tube, so that an exposed person is in more danger of acoustic trauma if he keeps the tube open by chewing and swallowing. [The more usual explanation of the outward burst of the drum head on exposure to blast is that it is caused by the suction exerted by the trough of negative pressure which follows the blast-wave.]

[This short but very important paper should be studied carefully.] *F. W. Watkyn-Thomas*

705. **Vocal Rehabilitation of Paralytic Dysphonia. I. Cartilage Injection into a Paralyzed Vocal Cord**
G. E. ARNOLD. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **62**, 1–17, July, 1955. 12 figs., bibliography.

Abductor paralysis of the vocal cord immobilizes it in the paramedian line. Phonation is only slightly disturbed, because the paralysed cord is in the position of phonation, but bilateral paralysis causes severe dyspnoea. Surgical methods of relief fix one cord in permanent abduction, so that the glottis is widened: thus respiratory improvement must mean weaker phonation, though many patients regain a " serviceable voice " by developing a new mechanism of phonation by means of a " pseudo-glottis " between the ventricular bands, between one cord and the opposite band, between a band and the opposing aryepiglottic fold, or between the descended epiglottis and the arytenoids. Adductor paralysis on the other hand leaves the glottis open so that there is no interference with respiration, but the glottis cannot be closed for normal phonation. Here again some patients compensate by developing the crossing-over of the healthy cord or using the " false cord " voice, but the result is usually not very good. If speech training and physiotherapeutic measures fail, three types of surgical procedure are available: (1) nerve anastomosis, (2) fixation of the paralysed cord in the middle line, and (3) injection of hard paraffin into the atrophic cord.

The results of this last operation on the whole have been good, but the paraffin causes a chronic foreign-body reaction with formation of granulation tissue (" paraffinoma "), and cases of embolism have occurred. Experiments were therefore begun in 1949 at New York University Post-Graduate Medical School to find an alternative material. Various kinds of cartilage—autogenous, heterogenous, fresh, and preserved—reduced to " crumbs " and suspended in procaine penicillin in oil to form a paste were first used. On the whole, however, procaine penicillin in oil proved unsuitable as a medium for suspension as, apart from provoking a foreign-body reaction, it may cause allergic complications, and experiments are now being made with saline–gelatin suspensions. Autogenous cartilage has the advantage that there is no need to use chemical preservatives; on the other hand in experiments on dogs and rabbits the heterogenous preserved material seemed to resist absorption better on injection into the thigh muscles. (This is contrary to the general experience of plastic surgeons, and may have been due to the method of preparation of the autogenous material.)

In 2 dogs the superior and inferior laryngeal nerves were divided on one side, and unilateral paralysis of the cord in the paramedian position was proved by repeated laryngoscopy, the resulting bark being very weak. After 15 to 20 weeks cartilage paste was injected into the paralysed and atrophic cord to bring it into the midline. In each case the dog recovered a good bark, and was well and healthy until killed some months later for examination of the larynx. An interesting point noted was that each dog developed acute tonsillitis on the side of injection immediately after the operation, the tonsil in the dog probably being a " regional lymphatic station " for the larynx. Further work is in progress.

F. W. Watkyn-Thomas

706. **Unilateral Vocal Cord Paralysis**
D. S. CUNNING. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol.* (*St Louis*)] **64**, 487–493, June, 1955. 4 refs.

During the 15-year period 1938–53 262 cases of unilateral vocal-cord paralysis were seen at the Manhattan Eye, Ear and Throat Hospital, New York, the right cord being involved in 82 cases and the left cord in 180. The cases could be divided according to causation as follows: trauma, including surgical accident, 21; mechanical causes from pressure in the chest or neck, 29; neoplastic disease, 72; toxic or inflammatory conditions, 58; and, lastly, 82 (31·3%) in which no cause could be found.

Of those due to toxic agents or acute upper respiratory infections, mobility of the cord was regained in the majority within 2 or 3 months. The author stresses, however, that the prognosis in these cases must be cautious. If there is an abductor paralysis control of the voice may be fairly good. On the other hand an adductor paralysis prevents opposition of the cords and the voice is poor in consequence. The author states that a course of speech therapy may do much to improve the quality of the voice in unilateral vocal-cord paralysis.

[On his own admission, however, he has little new to say.] *William McKenzie*

Urogenital System

707. **Electron Microscopy of the Vascular Bed of the Kidney Cortex**
D. C. PEASE. *Anatomical Record* [*Anat. Rec.*] **121**, 701–721, April, 1955. 17 figs., 14 refs.

This paper from the University of California School of Medicine and the Veterans Administration Center, Los Angeles, describes the preparation of, and findings in, electron micrographs of the glomerular capillaries of the kidney of the adolescent rat magnified 10 to 30,000 times, 17 of which are reproduced. Under pentobarbitone anaesthesia the kidney was brought to the exterior and stripped of its capsule, and a fixative (usually buffered 1% osmic acid) applied for about 90 minutes while blood was still circulating through the organ. The tissue was then dehydrated, embedded in butyl methacrylate, and suitably thin sections were cut with glass knives.

The epithelial cells of the glomerular capillaries have long primary branches extending over and between the capillary loops. From these, innumerable secondary branches emanate which alone are in direct contact with the basement membrane of the capillaries, interdigitating with one another and forming the external layer of the capillary wall. The endothelium in most parts of the glomerulus forms an extremely thin sheet of cytoplasm perforated by pores about 0·1 μ in diameter and very closely spaced. The basement membrane of the glomerular capillary is a continuous structure seemingly divisible into three layers, the middle, of high electron density, constituting the main structural element, with adjoining, low-density layers of cement substance attaching the endothelium on the one side and partially embedding the epithelial secondary branches on the other side.

The walls of the peritubular capillaries are also fenestrated, the thin endothelial sheet being perforated by a system of pores 0·04 to 0·05 μ in diameter, more widely and less regularly spaced than those of the glomerular endothelium, while the basement membrane is extremely thin; a cement layer can be seen. *L. H. Worth*

708. **Electron Microscopy of the Tubular Cells of the Kidney Cortex**
D. C. PEASE. *Anatomical Record* [*Anat. Rec.*] **121**, 723–743, April, 1955. 10 figs., 13 refs.

In this paper the findings in electron micrographs of the tubular cells of the rat kidney, prepared as previously described [see Abstract 707] are reported, with special reference to their basal portions and to the apical region of the proximal tubular cells. The surface membrane of the basal portion of these cells is elaborately infolded or invaginated to increase its surface area many times and has a fineness of structure far beyond the resolving power of the optical microscope. The infolded surface membrane forms a system of septa anastomosing freely with each other and not more than 27 mμ thick, the osmiophilic (lipid-containing) plasma membrane being 8 mμ thick, with a space 11 mμ thick between the two membranes forming each fold or septum. This system of infolded plasma membranes is only moderately developed in the cells of the proximal tubules.

The processes of the brush border at the apex of proximal tubular cells are apparently simple extensions of the apical cytoplasm. Variations in the amount of water in the apical ends of the cells of the proximal tubules, resulting from small variations in the procedure of fixation, cause major changes in the width of the tubular lumen and in the appearance of the apical cytoplasm, making the interpretation of the micrographic appearances rather difficult. Short cytoplasmic processes suggestive of a rudimentary brush border can be seen at the apical end of cells of the distal tubules and of the parietal cells of Bowman's capsule.

The basement membranes of the tubules appear to be entirely homogeneous. Sparse fibres are to be found only in the small connective-tissue spaces between tubules and capillaries. Granules, mostly of the basophilic, ribonucleic-acid type, are far more numerous in the cytoplasm of cells of the proximal than of the distal tubules. *L. H. Worth*

709. **Lower Nephron Nephrosis. I. A Pathogenesis for Degeneration of the Kidney Tubules. II. The Function of the Kidney when Tubular Degeneration Exists**
C. O. RICE, J. H. STRICKLER, and N. LUFKIN. *American Journal of Surgery* [*Amer. J. Surg.*] **90**, 547–557 and 558–561, Oct., 1955. 5 figs., 28 refs.

Balance studies were carried out on 102 patients after operation for a variety of severe major surgical conditions. A number of these patients died in the postoperative period and no adequate cause of death could be found at necropsy. Many of them, however, were found to have renal tubular degeneration of varying degree, and in all these cases the chemical studies carried out before death showed the presence of electrolyte imbalance. In a further 13 cases in which renal tubular degeneration was found electrolyte imbalance had also been present, but in these there were other post-mortem findings which adequately accounted for death.

The authors imply that "electrolyte imbalance" may produce tubular degeneration and that this combination seems to play a part in the pathogenesis of lower nephron nephrosis. They found in some cases that when the tubules were damaged anuria was not invariably present, although there was a decrease in urinary excretion of sodium and chloride and to a lesser extent of potassium and nitrogen. In many cases there was a marked rise in the blood sugar level, and its prompt depression by administration of insulin and glucose was in some cases life-saving. *G. A. Smart*

Endocrinology

710. **The Houssay Phenomenon in Man**
J. C. HARVEY and J. DE KLERK. *American Journal of Medicine* [*Amer. J. Med.*] **19**, 327–336, Sept., 1955. 2 figs., 29 refs.

In this paper from the Johns Hopkins Hospital, Baltimore, 3 cases of the Houssay phenomenon are described and 11 cases from the literature are briefly reviewed. At necropsy in 2 of the present cases changes were observed in the anterior pituitary gland—scarring subsequent to infarction in one case and abscess formation in the other. In one female patient, who had had diabetes for 9 years, hypoglycaemic attacks developed in the ninth month of pregnancy. A few days after admission to hospital she was delivered of a stillborn infant, and 2½ weeks later she died. During this time in hospital there were recurrent hypoglycaemic attacks although insulin administration had been stopped before delivery of the child. Another patient—with generalized sarcoidosis—was still alive at the time of the report [the clinical features in this case may possibly have been due to adrenal involvement].

The authors emphasize that this anterior-pituitary insufficiency syndrome should be considered immediately in all cases of diabetes in which there are increased sensitivity to insulin and subsequent hypoglycaemic coma.

I. McLean Baird

711. **A Case of von Recklinghausen's Disease with Pubertas Praecox.** (Случай болезни Реклингаузена с проявлениями раннего физического и полового развития)
D. D. SOKOLOV. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **1**, 96–99, No. 4, July–Aug., 1955. 2 figs., 6 refs.

Two theories of the causation of von Recklinghausen's disease have been put forward: one that it is due to a developmental error affecting mesodermal and ectodermal tissues, and the other that it is a multiple endocrine disturbance. The former view is supported by the presence in many cases of teratomata and deformities and errors of development in skeletal and other tissues; the latter by the frequent presence of signs of endocrine imbalance. However, the proof that such endocrine disorders are primary and not secondary is not usually forthcoming, as is illustrated in the case reported in this paper.

A boy of 16, seen at the All-Union Institute of Endocrinology, Moscow, with precocious physical and sexual development was found to have pigmented moles of the back of the head, right elbow, and wrist, and nodules in the iris of both eyes. His parents declared that the appearance of the moles had preceded the onset of abnormal growth, which they first noticed when the patient was 8 years old. Further nodules appeared subsequently on the back, chest, and abdomen; they were of a brown colour, and varied in size from that of a pin's head to several centimetres in diameter. The boy's skeleton was powerfully developed, the ossification advanced for his years, the skull massive, and the supra-orbital processes strongly developed, his build being that of a youth of 18. The external genitalia were those of a mature male, except that the left testis had not descended even to the inguinal canal. The radiographic appearance of the bones was suggestive of acromegaly, but there was no destruction of the processes of the sella turcica. The thyroid and parathyroid glands were apparently normal. The blood pressure was 145/70 mm. Hg.

The patient was regarded as having hyperadrenalism in view of his physical and sexual precocity, high blood pressure, hirsutism, and acceleration of the process of ossification. Since he had had signs of von Recklinghausen's disease before these endocrine symptoms appeared, the author considers that the latter were the result of stimulation of pituitary secretion of corticotrophin by a neurofibroma of the nervous tissue of the hypophysis.

[Although this case affords no proof of a primary endocrine disorder in von Recklinghausen's disease, the two series of phenomena appeared so soon after one another that the author's conclusion that the endocrine changes were secondary is equally difficult to uphold.]

L. Firman-Edwards

712. **Calcium Balance and Urinary Calcium Content in Acromegalic Decalcification.** (Bilans calciques et calciurie dans les décalcifications de l'acromégalie)
S. DE SÈZE, A. LIGHTWITZ, D. HIOCO, M. DELAVILLE, and H. GILLE. *Annales d'endocrinologie* [*Ann. Endocr. (Paris)*] **16**, 334–347, 1955. 13 refs.

In 4 cases of acromegalic decalcification studied at the Hôpital Lariboisière, Paris, osteoporosis and a negative calcium balance were accompanied by high blood calcium, phosphorus, and alkaline-phosphatase levels and increased urinary calcium and phosphorus output. The faecal calcium content was not markedly abnormal, and it is suggested that estimation of the urinary calcium level might well replace the laborious determination of calcium balance as an index of the state of calcium metabolism in these cases. Injection of oestrogens in 3 cases caused some reduction in urinary calcium output. Treatment with 150 mg. of cortisone daily in one case increased the negative calcium balance, which became positive on treatment with testosterone (100 mg. daily) or oestradiol (10 mg. daily) for 4 days. A positive balance was maintained for a short time after treatment with testosterone. The effect of cortisone was largely to increase faecal calcium output, that of androgens and oestrogens to diminish urinary calcium output.

F. W. Chattaway

713. **The Prothrombin-forming Function of the Liver and the Haemorrhagic Syndrome in Thyrotoxicosis.** (Протромбинообразовательная функция печени и геморрагический синдром при тиреотоксикозах)
M. A. ALEKPEROV. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **1**, 33–36, No. 4, July–Aug., 1955. 4 refs.

Determination of the prothrombin level in the blood can be used as a measure of hepatic function. The test is carried out before and after a loading dose of " visakol " (vitamin K_3). The prothrombin-forming function of the liver can be regarded as deficient when a subnormal level of prothrombin in the blood is not raised to normal by the loading dose. Normal levels are 85% or more. For the test described by the author anti-rabies vaccine was used as the source of thromboplastin.

A total of 100 cases of thyrotoxicosis were investigated, of which 36 were severe, 61 moderate, and 3 mild. In the severe cases the initial prothrombin index varied from 23·6 to 77% (average 51·7%); in the moderate cases it varied from 40·7 to 87·5% (average 65·9%), and in the mild cases from 74·4 to 89% [average not given]. The prothrombin index does not vary in proportion to the basal metabolic rate nor to the size of the thyroid gland or age or sex of the patient, but to the severity of the symptoms and the duration of the disease. Successful treatment, medical or surgical, of the thyrotoxicosis leads to a normalization of the prothrombin levels. A low prothrombin index is often accompanied by the development of the haemorrhagic syndrome, as evidenced by the " shoulder-strap " sign [presumably a purpuric staining in this region]. This sign appeared in 19 of the severe cases and 13 of the moderate cases of thyrotoxicosis in the series.

L. Firman-Edwards

ADRENAL GLANDS

714. **Biological Effects of Aldosterone with Especial Reference to Man**
F. T. G. PRUNTY, R. R. MCSWINEY, and I. H. MILLS. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 629–632, Aug., 1955. 2 figs., 15 refs.

The therapeutic effects of aldosterone, particularly in Addison's disease, are discussed. In one case of Addison's disease the metabolic changes and weight loss which followed complete withdrawal of conventional treatment were reversed by administration of aldosterone in a dosage of 200 μg. daily for 3 days followed by 400 μg. daily for 2 days. During the 5 days' treatment there was no noticeable effect on pigmentation or blood pressure. Sodium and chloride retention occurred, but sodium was retained in excess of the chloride, suggesting the possibility of intracellular transfer of sodium. Potassium balance was not affected, but there was a more positive water balance and even a slight increase in weight. In a girl with adrenal hyperplasia leading to pseudohermaphroditism who received more than double the dosage of aldosterone given to the first patient similar results were obtained, except that there was a significant change in potassium balance, involving rebound retention. Nitrogen excretion was not increased in either of these 2 cases. Aldosterone was found to be most effective when given by intramuscular injection, less effective when given by intravenous infusion, and least effective by mouth. In another case of Addison's disease 225 μg. of aldosterone intravenously resulted in sodium retention which was a little less than that produced by 5 mg. of DCA (deoxycortone acetate). The latter drug had less effect on potassium excretion than aldosterone. In all the cases there was definite evidence of water retention in response to aldosterone. The eosinophil count, the fasting blood sugar level, and insulin tolerance were uninfluenced by the drug.

P. A. Nasmyth

715. **Observations on the Regulatory Mechanisms of Aldosterone Secretion in Man**
J. C. BECK, I. DYRENFURTH, C. GIROUD, and E. H. VENNING. *Archives of Internal Medicine* [*Arch. intern. Med.*] **96**, 463–469, Oct., 1955. 4 figs., 12 refs.

716. **Metabolic Response to Total Adrenalectomy and Hypophysectomy**
A. S. MASON. *Lancet* [*Lancet*] **2**, 632–636, Sept. 24, 1955. 7 figs., 11 refs.

The metabolism of patients after adrenalectomy or hypophysectomy in the treatment of carcinomatosis was studied at the London Hospital to determine whether the characteristic postoperative responses—sodium retention, potassium loss, and nitrogen loss with subsequent regain—occur in the absence of the pituitary or the adrenal glands. Balance studies were carried out on 8 patients with carcinoma of the breast, 2 of whom had undergone total hypophysectomy, one total adrenalectomy, and 5 both total adrenalectomy and oophorectomy. In the 2 cases of total hypophysectomy the normal postoperative response was obtained when substitution therapy with a constant daily dosage of corticotrophin was given. Similarly, in the remaining patients the metabolic response was normal so long as the daily dosage of cortisone was maintained.

These results in the human subject thus confirm the experimental findings of Ingle (*J. Endocr.*, 1951, **8**, 23) that postoperative metabolic changes do not depend solely on alterations in adrenocortical activity.

C. L. Cope

717. **Metabolic Effects of 9α-Fluorohydrocortisone and of Cortisone in Adrenal Insufficiency**
O. GARROD, J. D. N. NABARRO, G. L. S. PAWAN, and G. WALKER. *Lancet* [*Lancet*] **2**, 367–370, Aug. 20, 1955. 5 figs., 20 refs.

The authors of this paper from the Middlesex Hospital, London, describe a study of the metabolic effects of 9α-fluorohydrocortisone (FHC) and of cortisone when given to 2 women, aged 51 and 53 respectively, with adrenal insufficiency, the first after total adrenalectomy for mammary carcinoma and the second with long-standing Addison's disease. The patients received a constant diet with added sodium and potassium, the composition of the diet being determined by analysis of samples. Water intake was measured but not restricted.

Cortisone was given by mouth in doses of 50 or 25 mg. daily, and FHC by mouth in doses of 1·0 or 0·5 mg. daily, the drugs being administered both separately and in combination.

On changing from cortisone to FHC there was a prompt retention of sodium accompanied by water retention, haemodilution (as shown by decreased haematocrit and plasma protein values), and a rise in plasma sodium with a fall in plasma potassium levels. When cortisone was substituted for FHC a sodium diuresis with loss of weight and reversal of the plasma changes occurred. It was concluded that 0·5 mg. of FHC had greater effect on electrolytes than 50 mg. of cortisone. When 0·5 mg. of FHC was given in place of 50 mg. of cortisone the T wave in the electrocardiogram became flattened, the mean eosinophil count rose, mean fasting blood sugar levels fell, and the ability to excrete a water load was decreased. This led to the conclusion that the glucocorticoid effects of 0·5 mg. of FHC were less than those of 50 mg. of cortisone.

The authors suggest that the combination of small doses of FHC with 20 to 25 mg. of cortisone daily may prove a satisfactory maintenance regimen in patients with adrenal insufficiency. *Charles Rolland*

718. **The Influence of ACTH and Cortisone on Certain Aspects of Aseptic Inflammation.** (Влияние адренокортикотропного гормона передней доли гипофиза и кортизона на некоторые стороны экспериментального асептического воспаления)
N. P. Smirnov. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **1**, 81–88, No. 4, July–Aug., 1955. 1 fig., 3 refs.

The author reports that ACTH in doses of 2 units per kg. body weight twice daily retarded the appearance and hastened the absorption of inflammatory exudate in experimentally induced aseptic inflammation in the ears of rabbits; the inflammation was provoked by applying water at an initial temperature of 60° C. The volume of the ear was measured before and again at 5 and 24 hours after the trauma, and thereafter daily for 7 days. In some of the experiments, the content of hyaluronidase in the exudate was determined by McClean's method, as modified by Smirnova. In control animals, the volume of the ear reached double its initial figure in 24 hours, then slowly diminished, but rarely returned to the initial volume within 7 days. In the majority of the animals treated with ACTH, the increase in size of the inflamed ears was less than double their initial volume (average 179·3%) and in all but 2 of 14 animals they had returned to normal size within a week.

In another series of experiments, in which 5 units of ACTH per kg. body weight was administered on the 4th day after trauma, similar results were obtained; but if this dose of ACTH was given at the time of the injury, the period of exudation was prolonged, and the ear volume at the end of 7 days was higher (119%) than in the control animals (113%). Finally, 5 units of ACTH per kg. was given daily from the time of injury, together with 10 mg. of cortisone per kg. from the fourth day. This addition of cortisone abolished the delay in reabsorption of exudates, and at the end of 7 days the volume of the ear was normal.

The explanation of these phenomena offered by the author is that repeated large doses of ACTH depress the function of the adrenal glands, thus actually suppressing the secretion of cortisone-like steroids. The effect of cortisone depends on the suppression or destruction of hyaluronidase, and consequent diminished permeability of the capillaries. This theory is supported by the results of estimations of hyaluronidase in the exudate from the ears of three groups each of 12 rabbits, of which one served as a control, one was given 5 units of ACTH, and the third was given a preparation of ACTH which was inactive to biological tests. The content of hyaluronidase in 1 ml. of exudate was 11·8, 6·5, and 9·3% in the three groups respectively, while the ear volume at the same time, that is, 5 hours after injury, was 214·7, 159·2, and 198·3% of normal respectively.

[It is a pity that this last experiment was not extended to the animals receiving cortisone in addition to ACTH, and also to all groups at a somewhat later period of inflammation.] *L. Firman-Edwards*

719. **Phentolamine in the Diagnosis and Management of Phaeochromocytoma**
E. P. W. Helps, K. C. Robinson, and E. J. Ross. *Lancet* [*Lancet*] **2**, 267–273, Aug. 6, 1955. 6 figs., 39 refs.

The value of phentolamine (" rogitine "), a derivative of tolazoline and an adrenolytic agent, in the differentiation of cases of phaeochromocytoma from essential hypertension and in the control of blood pressure during surgical removal of the tumour is discussed in this paper from University College and Whittington Hospitals, London. The technique employed for the phentolamine test and the management of 3 cases of phaeochromocytoma are described in detail.

The authors point out that phentolamine can be used for purposes of diagnosis only in patients with sustained hypertension. A fall in blood pressure of 35/25 mm. Hg or more, lasting for at least 5 minutes after injection of the drug, is considered to indicate a positive response. In the authors' cases the blood pressure fell to normal after the injection. False positive and false negative responses occur, particularly if the test is performed on patients in uraemia or during barbiturate sedation; the authors have encountered only one false positive response. When the response is positive or doubtfully positive the pressor-amine content of the urine should be assayed. The chief advantages of the phentolamine test are that there are no subjective symptoms other than tachycardia and the technique is simple and safe so that it can be carried out in the surgery or out-patient department. In 2 of the authors' cases there was a negative response to the piperoxane test and a positive response to phentolamine.

Phaeochromocytoma should be removed surgically, but unless an adrenolytic agent is given there is a violent rise in blood pressure, which may be fatal. The authors recommend the setting up of an intravenous infusion apparatus which will deliver 5% glucose (to keep the vein open), noradrenaline (4 mg. per litre of 5% glucose),

and phentolamine as necessary. Before induction of anaesthesia 5 mg. of phentolamine is given and during the operation 2 to 10 mg. is administered whenever the systolic blood pressure rises above 150 mm. Hg. After the tumour has been removed noradrenaline is given to maintain the blood pressure during the succeeding 24 hours, after which time noradrenaline is gradually withdrawn. A return of the hypertension after the operation with a fall in blood pressure in response to a further dose of phentolamine suggests that a second tumour is present, and this should be searched for. During the operation a minimum amount of phentolamine should be given, and phenylephrine should be available to combat acute hypotension unresponsive to noradrenaline.

A. Gordon Beckett

DIABETES MELLITUS

720. **Ocular Nerve Palsy with Severe Headache in Diabetics**

W. P. U. JACKSON. *British Medical Journal* [*Brit. med. J.*] 2, 408–409, Aug. 13, 1955. 13 refs.

Four cases are reported of severe localized headache with ocular-nerve palsies occurring in diabetic patients. In each case a "congenital" intracranial supraclinoid aneurysm (or similar local lesion) was suspected, but was not found, and the condition always disappeared within a few weeks. I believe it to be a variety of diabetic neuropathy, although I do not claim to have proved this.—[Author's summary.]

721. **Hypophysectomy in Man. Further Experiences in Severe Diabetes Mellitus**

R. LUFT, H. OLIVECRONA, D. IKKOS, T. KORNERUP, and H. LJUNGGREN. *British Medical Journal* [*Brit. med. J.*] 2, 752–756, Sept. 24, 1955. 3 figs., 5 refs.

In an attempt to arrest the progress of the vascular complications of severe diabetes, the authors, at Serafimerlasarettet and Karolinska Sjukhuset, Stockholm, performed hypophysectomy in young adult diabetics, and in this paper they report the results of this treatment in 20 patients (10 males and 10 females) aged 20 to 30 years with a diabetic history of 13 to 22 years. Diabetic retinopathy was present in all, and diastolic blood pressure was over 90 mm. Hg in 16. Two patients died within a week of the operation, 2 died at one month, and one at 6 months. Regular substitution therapy included administration of insulin, thyroxine, oestrogenic or androgenic hormones, and adrenocortical hormone. No clinical or laboratory evidence of acidosis was observed. Follow-up was possible in 12 cases for periods of 3 to 43 months. Some decrease in blood pressure occurred after operation, but in 2 cases pressure had risen to the high preoperative level at the end of 12 months' observation. It was found that the heart tended to decrease in size, that arterial calcification was unaffected, and that in all cases albuminuria diminished. There was reduction in the glomerular filtration rate but effective renal plasma flow was unchanged, the latter being considered a favourable result of the operation. No evidence of progression of renal disease was noted in any of the cases. Visual acuity improved in some, but was unchanged in 4, and in most cases there was improvement in the fundal appearances. Progression of the diabetic retinopathy occurred in only one case.

C. L. Cope

722. **Plasma-insulin Activity in Diabetes Mellitus, Measured by the Rat Diaphragm Technique**

J. VALLANCE-OWEN, B. HURLOCK, and N. W. PLEASE. *Lancet* [*Lancet*] 2, 583–587, Sept. 17, 1955. 16 refs.

The authors have measured the effective plasma insulin concentration of diabetic patients, using the method based on the glucose uptake of the isolated rat diaphragm. Various points in favour of the argument that the plasma insulin activity—that is, the resultant of insulin and its antagonists—is actually estimated by the technique are considered; the accuracy of measurement and sources of error in the method are also discussed. The experimental procedure has been previously described (*Lancet*, 1954, **1**, 68); it is based on a comparison of the uptake of glucose from undiluted plasma with that from a buffer solution of ionic composition similar to plasma, with or without the addition of insulin.

The diabetic patients were chosen at random and separated into two main groups according to whether or not they were receiving insulin. From the latter group (17 patients) blood specimens were taken for estimation of plasma insulin after a 12-hour fast, and in most cases a further blood sample was obtained one hour after administration of 50 g. glucose by mouth. Insulin activity was found in the plasma of all 17 patients, and this was increased after administration of glucose. The mean fasting level was higher than that previously reported for normal fasting subjects (loc. cit.). An independent clinical assessment of the type of diabetes in these patients showed that 15 were typically obese diabetics, one had been obese but was ultimately given a small dose of insulin, and the remaining patient was thin but showed a decline in the fasting blood sugar level and glycosuria on a low-carbohydrate diet.

From the group receiving insulin treatment (27 patients) blood specimens for plasma insulin estimation were obtained either after a 12-hour fast and before the morning dose of insulin, or an hour after the morning injection of insulin and about 30 minutes before breakfast. In 20 of these patients no plasma insulin activity was detected, whether the blood was removed during fasting or after the morning dose of insulin. The blood sugar levels of this group ranged between 170 and 475 mg. per 100 ml. The remaining patients had blood sugar levels within the normal range and also showed plasma insulin activity. Two patients were studied on two separate occasions; on the first the blood sugar level was raised and there was no plasma insulin activity, and on the second the blood sugar level was physiological and insulin activity was found in the plasma. None of the patients receiving insulin had ketonuria on the day of the test. A later clinical study of the 20 patients with no plasma insulin activity and a raised blood sugar level

showed that 18 were thin and had ketonuria when insulin was withheld—" they were typical ' insulin-requiring ' diabetics ".

Experiments were also made on the recovery of a known amount of insulin added *in vitro* to the plasma of diabetic patients. The insulin was satisfactorily recovered from the plasma of the obese group, but not from that of the " insulin-requiring " group whose blood sugar levels were above the normal range. However, from the plasma of the " insulin-requiring " patients with blood sugar levels within the normal range the added insulin was again satisfactorily recovered.

[The present results are of importance in that they indicate a metabolic difference between the two broad types of clinical diabetes, and thereby provide confirmation of earlier work in which a different method of estimating insulin activity was used (*Brit. med. J.*, 1951, **1** 732; **2**, 1541). However, the rat-diaphragm method determines only the glucose uptake, and the statement that it measures the effective insulin concentration in plasma must be accepted with caution. A recent communication (*Lancet*, 1955, **2**, 775) has criticized this assumption, and more exact studies of the factors responsible for the activity of plasma in the rat-diaphragm preparation are necessary before any firm conclusions can be drawn (see also *Brit. med. J.*, 1954, **1**, 1237; *Abstracts of World Medicine*, 1954, **16**, 268).]

M. J. H. Smith

723. **Diabetes Mellitus and Liver Function**

R. F. Bradley, U. Sagild, and F. E. Schertenleib. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 454–458, Sept. 15, 1955. Bibliography.

Much has been written concerning liver function in patients with diabetes mellitus. On the whole, liver function tests and examination of biopsy specimens and of the liver post mortem have failed to reveal any significant abnormalities in well-controlled diabetes. The authors review the extensive literature on the subject, and report the results of their own investigations at the New England Deaconess Hospital and Joslin Clinic, Boston, in 118 diabetic patients. Their group was unusual only in the preponderance of males (76), all those with a history of unrelated liver disease, malnutrition, and recent ketosis being excluded. The liver function tests, which were performed in the first few days after admission when there was still some variation in diabetic control, included thymol turbidity and flocculation, cephalin–cholesterol flocculation, and estimation of serum bilirubin level and " bromsulphalein " retention.

In 16 patients the results of one or more of these tests were abnormal and in 6 the results of two or more were abnormal. Bromsulphalein retention, considered to be the most sensitive index of liver function in this series, was slightly increased in 12 cases. The duration of the diabetes in no way influenced the results of the liver function tests. The authors conclude that the low incidence of abnormal liver function in this series indicates that significant liver disease " occurs rarely as a result merely of the presence of diabetes mellitus ".

J. N. Harris-Jones

724. **Lipoid-Amyloid Nephrosis and Juvenile Diabetes Mellitus.** (Липоидно-амилоидный нефроз и юношеский сахарный диабет)

E. Y. Reznitskaya. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **1**, 100–102, No. 4, July–Aug., 1955. 1 fig., 32 refs.

In spite of the high incidence of active tuberculosis, pyogenic infections, and hyperlipaemia in uncontrolled diabetes, lipoid–amyloid nephrosis is rarely observed in such cases. The possibility that the perverted metabolism and reactivity in diabetes may account for abnormalities in the course of diseases accompanying or complicating it is illustrated by a case reported here from the Astrakhan Medical Institute.

The patient, a 13-year-old boy, was admitted with general weakness, headache, oedema of the face and body, pyrexia, and oliguria which had followed a recent period of polyuria. Two years previously he had had severe malaria, and diabetes had been diagnosed at that time. Antimalarial treatment had been carried out irregularly, and he had received 10 to 20 units of insulin twice daily with a diet reduced almost to starvation level. The oedema had started to develop 2 months before admission. He had intense albuminuria, and the urinary deposit contained leucocytes, a few erythrocytes, and hyaline and granular casts. *X*-ray examination revealed a wedge-shaped shadow in the middle-lobe region of the right lung. There was a mild hypochromic anaemia with leucopenia and a monocytosis of 12%. The plasma cholesterol level was 450 mg. per 100 ml. The diagnosis of lipoid–amyloid nephrosis was made from the result of the Congo-red test. At this time the blood glucose level was only 109 mg. per 100 ml., but after a few days of a high-carbohydrate, high-insulin regimen it rose to 280 mg. per 100 ml. Tuberculosis was suspected, but tubercle bacilli were not found in sputum, urine, or stools. Streptomycin treatment aggravated his already serious condition and was discontinued after 2 days.

A low-water, low-salt, low-fat (30 g.) diet with a high content of protein (90 g.), carbohydrate (600 g.), and vitamins and a total value of 3,000 Calories was prescribed. Once a week the patient received abundant fruit, sweets, kephir (fermented milk), honey, and sugar with a high insulin dosage (up to 180 units a day in 3 doses). At the same time he was given antimalarial treatment, mercurial diuretics, thyroid extract, transfusions of serum, diathermy to the renal area, and penicillin. With this complex treatment he rapidly improved, the oedema subsiding and the albuminuria diminishing (to disappear entirely within a year); at the same time glucose appeared in the urine, from which it had been absent during the period of acute nephrosis. The diabetes was stabilized with an adequate diet and 20 to 30 units of insulin twice daily. He has been under observation for 3 years and appears to be doing well.

L. Firman-Edwards

725. **Urinary Excretion of Acid Mucopolysaccharides by Diabetic Patients**

J. G. Craddock and G. P. Kerby. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 193–198, Aug., 1955. 1 fig., 11 refs.

The Rheumatic Diseases

726. **Variations of Beta Glucuronidase Concentration in Abnormal Human Synovial Fluid**
R. F. JACOX and A. FELDMAHN. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 263–267, Feb., 1955. 2 figs., 6 refs.

The importance in mucin metabolism of the enzyme β glucuronidase, which splits conjugated glucuronides, prompted the present study, reported from the University of Rochester, New York, of the concentration of the enzyme in synovial fluid. Using a modification of the method of glucuronidase assay described by Talalay *et al.* (*J. biol. Chem.*, 1946, **166**, 757), the authors estimated the enzyme content of fluid from joints affected by a variety of pathological conditions in 56 cases. They found a very high concentration in synovial fluid from patients suffering from pyogenic arthritis, a moderate yield in some cases of rheumatoid arthritis, and a low yield in cases of degenerative arthritis. Synovial fluid with a high cell content tended to have a high β-glucuronidase content, but the correlation was not absolutely linear. The concentration of the enzyme was reduced after removal of the cells by centrifugation and, although synovial secretion cannot be excluded, the enzyme is probably derived from disintegrated leucocytes.

In 3 cases, one of pyogenic, one of rheumatoid, and one of degenerative arthritis, serial determinations of the β-glucuronidase content of the synovial fluid were made. The level was very high in the initial phase in the case of pyogenic arthritis and subsequently appeared to vary with the degree of activity. Similarly in the case of rheumatoid arthritis there was a high correlation between the enzyme content and the clinical assessment of activity. In the case of degenerative joint disease the initial level was low and no appreciable change was observed over a period of study of 170 days. The estimation of the β-glucuronidase content of the synovial fluid would not appear to have any specific diagnostic value, but it appears to reflect the cellular response to the inflammatory change in the synovial membrane and, once the diagnosis is made in cases of rheumatoid arthritis, serial determinations might afford a possible guide to changes in the degree of activity. *R. E. Tunbridge*

727. **Anti-rheumatic Potency of Butazolidin in Low Doses**
M. KELLY. *British Journal of Physical Medicine* [*Brit. J. phys. Med.*] **18**, 191–196, Sept., 1955. 2 figs., 7 refs.

The author gives his personal experience with phenylbutazone ("butazolidin") in the treatment of 800 patients with various rheumatic conditions over a period of 3 years. He considers it to be a specifically anti-rheumatic drug which is not dangerous if given in correct dosage to suitable patients. Patients over the age of 65 and those with chronic diseases of the blood, kidneys, cardiovascular system, or alimentary tract should be excluded. He recommends that a dose of 0·6 g. should not be given for more than 2 days at a time and 0·4 g. for not more than a week, and states that 0·2 or 0·3 g. is usually a sufficient maintenance dose. The toxic effects, if any, nearly always occur during the first 4 weeks of treatment, and the patient should be instructed to watch for them and told to stop the drug if any occur. Patients who receive no benefit from the drug at first may respond to a second or third trial.

The author stresses that phenylbutazone is not an analgesic, but is specifically anti-rheumatic in action, the mechanism whereby it surpresses rheumatic inflammation remaining unknown. *Oswald Savage*

728. **The Toxic Effects of Phenylbutazone (Butazolidin): Review of the Literature and Report of the Twenty-third Death following Its Use**
E. F. MAUER. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 404–410, Sept. 8, 1955. 2 figs., bibliography.

729. **The Use of "Metacortandracin" [Prednisone] and 9-α-Fluorohydrocortisone Acetate in the Rheumatic Diseases.** (L'impiego del metacortandracin e del 9-α-fluoroidrocortisone acetato nelle malattie reumatiche)
C. B. BALLABIO, A. AMIRA, E. CIRLA, and G. SALA. *Reumatismo* [*Reumatismo*] **7**, 113–126, May–June, 1955. 9 figs., 5 refs.

At the Centre of Rheumatology of the University of Milan 14 patients (9 males and 5 females ranging in age from 7 to 71) suffering from rheumatoid arthritis (7 cases) or other rheumatic disorders were treated with prednisone ("metacortandracin") or 9-α-fluorohydrocortisone. Most of them had previously been treated with cortisone or hydrocortisone, ACTH, or phenylbutazone. Both drugs were given by mouth, the initial dose being 30 to 50 mg. for prednisone and 8 to 16 mg. for 9-α-fluorohydrocortisone. The duration of treatment varied according to experimental requirements, but in some cases the same scheme of treatment was used as with cortisone.

Both steroids showed a definite anti-rheumatic effect, prednisone proving 3 to 4 times more effective than cortisone, and 9-α-fluorohydrocortisone 8 to 10 times more active. Salt and water metabolism was not influenced by prednisone but was much disturbed by 9-α-fluorohydrocortisone, which caused oedema with salt and water retention. For that reason the latter was regarded as unsuitable for clinical use. Both steroids produced signs of hyperadrenalism, varying in degree with the dosage and length of treatment and similar to those caused by cortisone and hydrocortisone. The authors stress the practical importance of the absence of any effect of prednisone on fluid balance, making it suitable even for patients with a failing heart. *V. C. Medvei*

730. **The Effect of Intensive and Prolonged Therapy with Cortisone and Hydrocortisone in First Attacks of Rheumatic Carditis**

M. MARKOWITZ and A. G. KUTTNER. *Pediatrics* [*Pediatrics*] **16**, 325–334, Sept., 1955. 5 refs.

The effect was studied of prolonged administration of large doses of cortisone or hydrocortisone on the incidence of residual rheumatic heart disease in patients with carditis during a first attack of rheumatic fever, with particular reference to the incidence in patients treated within 3 weeks of the onset of symptoms and those treated 3 weeks or more after the onset. To ensure an adequate series a total of 40 patients was drawn from two clinics in New York and Baltimore, and the combined results are herein reported. The dosage of the drugs, which were given by mouth, was as follows: (1) 300 mg. of cortisone or hydrocortisone daily for 6 weeks, with gradual reduction over the next 3 weeks (10 patients); (2) 300 mg. of cortisone daily for 2 days, then 200 mg. daily for 40 days, followed by gradual reduction over the succeeding 3 weeks (8 patients); and (3) the same as in (2) except that after the period of gradual reduction a daily maintenance dose of 50 mg. of cortisone was given for 2 to 10 months (22 patients).

Of 29 patients treated within 3 weeks of the onset of the illness, 24 had no evidence of heart disease when examined 6 to 22 months later, compared with only 2 of the 11 treated more than 3 weeks after the onset. Serious side-effects developed in 11 of the 40 patients and were sufficiently severe in 4 to necessitate cessation of treatment. Hypertension was observed in 8 cases, in one of which blood pressure rose to 160/120 mm. Hg and the patient had a convulsion. In 4 cases there was stomatitis and in one multiple paronychia. One patient became euphoric and one developed headache and became semi-conscious. In every case, however, these side-effects were temporary, and there were no permanent personality changes.

The authors suggest that cortisone in large doses should be given early in the course of rheumatic fever and continued until the disease has run its course. They consider, however, that further studies based on a larger series of cases with adequate controls are needed to establish the value of this method of treatment.

K. C. Robinson

731. **Agglutinins and Incomplete Antibodies after a Single Antigenic Inoculation in Normal and Rheumatic Individuals**

V. WAGNER and V. REJHOLEC. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 243–250, Sept., 1955. 5 figs., 31 refs.

732. **Familial Occurrence of Ankylosing Spondylitis**

R. M. STECHER and A. H. HERSH. *British Journal of Physical Medicine* [*Brit. J. phys. Med.*] **18**, 176–183, Aug., 1955. 13 refs.

At the City Hospital (Western Reserve University), Cleveland, Ohio, the immediate relatives of 56 patients with ankylosing spondylitis were studied. Among 158 brothers and sisters, 6 further examples of the same condition were encountered, and among 108 parents, one was found to have the disease. This familial incidence was rather more than 10 times greater than that found in a series of 616 control families. It is thought that the condition is genetically determined and is probably due to a rare autosomal dominant gene with incomplete manifestation, the penetrance being calculated as about 70% in males and 10% or slightly more in females.

[The calculations carried out to determine the " penetrance " of the gene appear to the abstracter to be of doubtful validity.] *H. Harris*

RHEUMATOID ARTHRITIS

733. **Lung Lesions in Rheumatoid Arthritis**

A. ARONOFF, E. G. L. BYWATERS, and G. R. FEARNLEY. *British Medical Journal* [*Brit. med. J.*] **2**, 228–232, July 23, 1955. 4 figs., 26 refs.

After a brief review of reported cases of lung lesions in rheumatoid arthritis, the authors discuss their experience of such cases at the Postgraduate Medical School of London over the last 15 years. Of 253 patients with rheumatoid arthritis, 180 were free from chest disease; in the remainder the most common lesions were bronchitis (including pneumonia), bronchitis and emphysema, emphysema alone, bronchiectasis, and old apical tuberculosis. The authors point out that these findings are not very different from those to be expected in a general hospital population.

Radiological examination of the chest in these cases and in a control series revealed that the over-all incidence of lung disease was slightly higher in patients with rheumatoid arthritis than in the controls but that the changes in the two groups were similar. Moreover, at necropsy on 42 patients with rheumatoid arthritis no specific lung changes were found and no nodules were seen. *G. Loewi*

734. **A Comparison of Cortisone and Aspirin in the Treatment of Early Cases of Rheumatoid Arthritis. A Second Report**

MEDICAL RESEARCH COUNCIL/NUFFIELD FOUNDATION JOINT COMMITTEE ON CORTISONE, ACTH, AND OTHER THERAPEUTIC MEASURES IN CHRONIC RHEUMATIC DISEASES. *British Medical Journal* [*Brit. med. J.*] **2**, 695–700, Sept. 17, 1955.

The methods employed in this comparative therapeutic trial of cortisone and aspirin in early rheumatoid arthritis, and the results which were obtained during its first year, have already been reported (*Brit. med. J.*, 1954, **1**, 1223; *Abstracts of World Medicine*, 1954, **16**, 405). The present report records the results obtained up to the end of the second year. Of the original 61 patients suffering from rheumatoid arthritis of not more than 9 months' duration, 30 were treated with cortisone and 31 with aspirin. During the first year 3 patients were lost from the trial, but during the second year no losses occurred, and all 58 remaining patients were available for assessment, 30 having been treated with cortisone and 28 with aspirin. Continuous treatment

was given during the second year except in cases of remission, the dosage being left to the discretion of the physician, the aim being " to employ the minimum that would produce maximum functional efficiency and relief of symptoms without producing serious side-effects ". The effect of treatment on various aspects of the disease was assessed by simple objective methods, details of which are given, and the average results in the two groups at the end of the second year are here compared with those at the end of the first. (*a*) *Joint Tenderness*. The similarity between the results in the two groups after one year was confirmed after two years. (*b*) *Range of Movement and Strength of Grip*. Whereas in the first year the average degree of improvement with cortisone was greater than with aspirin, after the second year the gap had narrowed, and while both groups showed some uniform deterioration, there was no significant difference between them. (*c*) *Dexterity*. The results in the two groups remained very similar. (*d*) *Haemoglobin Level and Erythrocyte Sedimentation Rate*. Whereas the cortisone-treated group responded better than the aspirin-treated group in the first year, this advantage was not maintained during the second year, at the end of which the average figures for the two groups were remarkably similar. (*e*) *Clinical Assessments*. At the end of the second year 4 patients in each group were reported as being in remission. The assessments of clinical activity and of functional capacity in the two groups were " more remarkable for their similarity than for their dissimilarity ".

Assessment of the *x*-ray appearances of the hands, which was carried out only during the second year of treatment, was complicated by differences in the standards adopted by different observers. Although the mean gradings for osteoporosis and erosion were higher in the aspirin-treated than in the cortisone-treated group, the differences were not statistically significant. Where films taken before starting treatment were available for comparison it was found that there had been a marked, but similar, degree of progression of erosion, but not of porosis, in the two groups.

In discussing the findings the authors stress the remarkable similarity which now appears between the two groups. [But it must always be remembered that the trial is being carried out on selected, and not random, groups of cases of rheumatoid arthritis.]

W. Tegner

735. **The Treatment of Rheumatoid Arthritis with " Atebrin " [Mepacrine] and " Resochin ".** (Die Atebrin- und Resochin-Behandlung der progressiven Polyarthritis chronica)

J. Escarpenter-Oriol, A. Carreras Bayés, and M. Sariols Gomez. *Medizinische* [*Medizinische*] 1083–1086, No. 31/32, Aug. 6, 1955. 9 refs.

At the Medical Clinic B of the University of Barcelona the authors treated 15 patients with rheumatoid arthritis with 0·3 g. of mepacrine daily until yellow coloration of the skin appeared, and then with 0·2 g. daily for 2 to 3 months. Of the 8 patients who completed the course, 5 seemed to improve. All suffered from gastro-intestinal symptoms.

In a further series of 14 cases of moderately severe arthritis 500 to 750 mg. of " resochin " was given daily for 10 days, then on alternate days for a further 20 days, and finally 250 to 500 mg. on alternate days for 2 to 3 months. There was some improvement in all but one case and the erythrocyte sedimentation rate tended to fall. No signs of toxicity were noted.

[No control observations are reported; therefore no conclusions should be drawn.] *G. Loewi*

736. **Ulceration of the Skin in Rheumatoid Arthritis.** [In English]

V. A. I. Laine and K. J. Vainio. *Acta rheumatologica Scandinavica* [*Acta rheum. scand.*] **1**, 113–118, 1955. 3 figs., 3 refs.

Single or multiple ulceration of the skin was observed in 12 out of 2,000 cases of rheumatoid arthritis seen at the Hospital of the Rheumatism Foundation, Heinola, Finland. The site of the ulcers varied but was most frequently the lower part of the leg. In all except one case the ulcers developed near an affected joint. Ulceration was preceded by oedema, and appeared to follow the breakdown of a rheumatic nodule in the skin. Peripheral vascular disease played no part in causation of this condition.

Histological examination revealed a granuloma in the dermis with perivascular exudate; there was fibrinoid degeneration of the walls of the vessels. A frequent finding was a typical rheumatic nodule at the base of the ulcer showing fibrinoid necrosis surrounded by palisading histiocytes. The ulcers, which were resistant to treatment, developed during an acute exacerbation of the rheumatoid process and subsided spontaneously during a quiescent phase. *William Hughes*

737. **Gold and " Acton Prolongatum " in Rheumatoid Arthritis.** (Guld och acton prolongatum vid arthritis rheumatica)

G. Sebardt. *Nordisk Medicin* [*Nord. Med.*] **54**, 1277–1279, Aug. 18, 1955. 12 refs.

The results obtained in a series of 1,824 patients with rheumatoid arthritis treated at Umeå Hospital, Sweden, with " acton prolongatum ", a long-acting corticotrophin preparation, and observed for 1½ years are reported and compared with those in an earlier series of 1,086 patients treated with gold. The analysis shows that hormone therapy was, if anything, more effective than gold therapy, and the average duration of treatment shorter. Moreover, it eliminates the risk of serious complications which is associated with gold therapy. *L. Michaelis*

738. **Synovectomy of the Knee in Rheumatoid Arthritis. An Essay in Surgical Salvage**

P. S. London. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **37B**, 392–399, Aug., 1955. 6 figs., 22 refs.

An attempt is made to assess the value of synovectomy of the knee in rheumatoid arthritis from the results obtained in 34 joints operated on since 1946. Synovectomy was considered only when accepted medical and physical treatment had failed to control the pain

and swelling, and was not advised unless there was at least 45 degrees of movement and the disease had reached a relatively quiescent stage.

Usually the joint was exposed by a medial parapatellar incision dividing the quadriceps and its expansion vertically. The appearance of the joint varied considerably. A small, often semi-solid effusion was usually present. In some instances the synovial membrane was only slightly reddened and thickened, while in others it showed considerable thickening and occasionally polypoid hypertrophy. Erosion of articular cartilage was seldom marked, but the semilunar cartilages were often sufficiently diseased to require removal. The extent of the operation varied from partial synovectomy to extensive joint clearance, which in 2 cases included removal of the patella. Three weeks after operation the joint was manipulated under anaesthesia and active movements were begun.

Although as a result of the operation there was little change in the amount of joint movement permitted, the clinical state of most of the patients improved considerably. The late results were more favourable in joints showing little radiological change before the operation and possessing originally a good range of movement. Since it has been shown experimentally that the synovial membrane has considerable powers of regeneration, the final results may well depend upon the subsequent activity of the rheumatoid process. *Peter Ring*

739. **Multiple Intra-articular Injections of Hydrocortisone in the Treatment of Rheumatoid Arthritis.** (Sur les injections multiarticulaires d'hydrocortisone dans le traitement des polyarthrites chroniques évolutives)
R. Weismann-Netter, B. Krewer, and P. Lorch. *Presse médicale* [*Presse méd.*] **63**, 1153–1155, Sept. 3, 1955. 1 ref.

The authors describe their experience at the Hôpital Beaujon, Paris, with intra-articular injections of hydrocortisone acetate in the treatment of rheumatoid arthritis. Contrary to the opinion expressed by some workers that such treatment is especially suitable when only one or a few joints are affected, the authors have found the treatment particularly useful in polyarthritic cases. They describe the technique in detail. A general anaesthetic may be necessary, partly on account of the pain involved and partly because it relieves muscular spasm and makes access to the joint cavity easier. The amount injected depends on the size of the joint and degree of involvement: about 5 ml. of a solution containing 25 mg. of hydrocortisone per ml. is suitable for the knee, hip, or shoulder, while 1 ml. is an appropriate dose for the distal interphalangeal joints. A total dose of 2 to 2·5 g. may be injected in a single case. The Thorn test gives a negative result after the injections, and there is no change in the ketosteroid or electrolyte content of the blood. This suggests that the drug is not absorbed in any quantity from the site of injection. In these circumstances the authors report a complete absence of side-effects. They find that no dietary restrictions and no control of salt intake are necessary. Similarly, the usual contra-indications for cortisone therapy can be ignored, and they have given hydrocortisone with impunity in cases complicated by active tuberculosis and peptic ulcer. Relapse, they note, is inevitable within 6 weeks to 12 months and is treated by a repetition of the injections. They underline the importance of physiotherapy as an ancillary measure, and state that in many cases the patient can dispense with the use of analgesics immediately after treatment. They do not claim that the treatment is curative, even in the most suitable type of case, but they do insist that patients who were previously crippled and bedfast have been rendered mobile and free from pain. These results, even if temporary, justify a wider use of the treatment.

William Hughes

740. **Total Rehabilitation of the Rheumatoid Arthritic Cripple**
E. W. Lowman, P. R. Lee, and H. A. Rusk. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 1335–1344, Aug. 13, 1955. 8 figs., 11 refs.

The rehabilitation of patients disabled by rheumatoid arthritis is discussed with special reference to the results obtained over a recent 2-year period at the Goldwater Memorial Hospital, New York. With a combination of medical treatment and rehabilitation 7 out of 18 severely disabled patients became totally self-sufficient, one being well enough to undertake full-time employment. The average age in this group was 46 years and the average duration of the disease 13 years. Of 20 less severely disabled patients, 15 became totally self-sufficient, and 7 of these patients were eventually placed in full-time employment. Medical treatment, when considered necessary, consisted in administration of cortisone or hydrocortisone in a dosage of 15 to 25 mg. daily at first, increased gradually to the " lowest maintenance level capable of controlling the symptoms ". The duration of steroid therapy varied from 6 to 22 months, but in 2 cases this treatment was interrupted temporarily because of severe side-effects. In 6 patients relief of symptoms was obtained following a course of phenylbutazone.

Supportive psychotherapy was also employed, with the object of counteracting passivity and dependency. Functional training in rehabilitation was directed towards " maximum performance of activities essential to independent daily living ". Visits were paid to the patient's home to deal with any problems in the family situation or living conditions which might present difficulties after discharge from the protective environment of the hospital. Special apparatus was avoided except where necessary to achieve adequate function. Self-help devices included chairs and toilet seats raised above the standard height, elastic shoelaces, and long-handled shoe-horns. For reaching inaccessible parts of the room the patients had an all-purpose utility stick with multiple attachments, while for housewives there were adjustable ironing boards and work tables on castors. Splints or braces were used, especially for correction of knee-flexion deformity and for the prevention of wrist-drop and ulnar deviation of the hand.

A. Garland

Physical Medicine

741. **The Effectiveness of Microwave Diathermy Therapy as a Hyperthermic Agent upon Vascularized and Avascular Tissue**

A. W. RICHARDSON. *British Journal of Physical Medicine* [*Brit. J. phys. Med.*] **18**, 143–149, July, 1955. 6 figs., 17 refs.

A review of the literature on the effects of deep heating by means of various types of diathermy showed that a critical temperature of 43° C. was essential to produce a significant increase in local blood flow. In studies carried out at Indiana University School of Medicine, Bloomington, Indiana, the author has demonstrated that microwave diathermy can increase the rate of blood flow through peripheral skeletal muscle and also increase the tissue temperature. The apparatus used was a commercial 12·25-cm. (2,450 megacycles frequency) microwave generator with an output of 63 to 125 watts. Temperature was measured by a thermocouple in a hypodermic needle, and blood flow by an electromagnetic flow meter connected to the femoral artery.

In studies carried out *in vivo* on 12 mongrel dogs anaesthetized with pentobarbitone sodium, and also post mortem on the hind limbs of dogs or on freshly excised ox eyes, it was shown that the vascularized limbs had an increased blood flow (by 50 to 60%) as a result of heating; this increase required a hyperthermic threshold of 43° C. and continued after cessation of heating. It is stated that the increase in blood flow controls the degree of heating, and that in avascular tissue overheating occurs but can be prevented by the use of a 1-mm. mesh wire screen. In avascular optic tissue heated for 10 minutes a rise in temperature of 20° C. was obtained. The author discusses the mechanism of blood flow in relation to temperature changes.

J. B. Millard

742. **Use of Hyaluronidase by Iontophoresis in Treatment of Lymphedema**

M. S. SCHWARTZ. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 662–688, May, 1955 [received Aug., 1955]. 3 figs., 14 refs.

The effect of the administration of hyaluronidase by iontophoresis on chronic lymphoedema was studied at the New York University Hospital and Bellevue Hospital, New York, in 5 cases. To 250 ml. of 0·1 M acetate buffer solution at *p*H 5·4 was added 150 turbidity reducing units of hyaluronidase, and this freshly-prepared solution was applied on gauze to cover the lymphoedematous limb. The gauze was covered by a flexible tin electrode wound spirally, which served as the anode, and a current of 20 mA was passed for 20 to 30 minutes. The difference in volume of the limb before and after treatment was measured by a water-displacement method. The treatment was usually carried out weekly; in each case control treatments with the buffer solution only were interspersed at random among the treatments with hyaluronidase.

In each case it was found that while the control treatment had a negligible effect on limb volume, treatment with hyaluronidase resulted in a decrease in volume by an average of 140 to 290 ml. In 4 cases in which a leg was involved this reduction was maintained by firm bandaging between treatments, so that after 10 to 24 sessions the volume of the limb had been reduced by 800 to 2,000 ml. In the fifth case, in which an arm was affected and supportive bandaging was not carried out, little over-all reduction in volume was achieved. Two of the patients experienced a copious diuresis following treatment; no other side-effect was noted.

The author points out that although the ability of hyaluronidase administered in this way to increase the absorption of fluid from the skin and subcutaneous tissues appears to have been demonstrated, further studies will be necessary to determine whether prolonged reduction of lymphoedema can be achieved by this method.

B. E. W. Mace

743. **Rehabilitation of the Chronic Rheumatoid Arthritic: a Two-year Progress Report**

E. W. LOWMAN. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **36**, 431–434, July, 1955.

The effects of a programme of medical and rehabilitation treatment over a 2-year period on a selected group of 38 patients with active rheumatoid arthritis were studied at Goldwater Memorial Hospital (New York University), New York. The main criteria for selection were that the patient should be between 21 and 55 years old, with severe functional impairment, but not in obvious need of orthopaedic treatment, and with no medical contraindication for hormone therapy.

The patients' degree of incapacity was assessed according to the system of the American Rheumatism Association, the majority being placed in Classes III and IV, and also in relation to a list of over 100 activities considered necessary for self-sufficient daily living. On the basis of the latter assessment the patients were divided arbitrarily into (1) a "severely disabled" group (18 patients), and (2) a "less severely disabled" group (20 patients). The average age in Group 1 was 46 years and average duration of the disease 13 years, the corresponding figures in Group 2 being 40 years and 7 years respectively. Treatment with cortisone or hydrocortisone was necessary "to control the activity of the rheumatic process" in 25 out of the 38 cases. Salicylates alone were sufficient for this purpose in 5 cases, and phenylbutazone alone in 8. [No details of the programme of rehabilitation are given, but see Rheumatic Diseases, Abstract 740.]

The results were encouraging. Of the 18 patients in Group 1, 14 were discharged from hospital [presumably to continue maintenance therapy] after about 11 months, 7 being self-sufficient and 7 partially self-sufficient at that time, and one of these was able to take a full-time job; the 4 remaining patients needed continued hospital

care. The average improvement in functional capacity (as judged from ability to perform the activities mentioned above) was 28% in this group. The patients in Group 2 were discharged from hospital after an average stay of 7 months; 15 were self-sufficient at that time, and 7 of these were placed in full-time employment. The average functional improvement in this group was 30%.

J. B. Millard

744. **Use of Ultrasonic Vibration in the Treatment of Pain Arising from Phantom Limbs, Scars and Neuromas: a Preliminary Report**

D. RUBIN and J. H. KUITERT. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **36**, 445–452, July, 1955. 2 figs., 18 refs.

At Brook Army Hospital, Fort Sam Houston, Texas, ultrasonic therapy was applied locally in the treatment of 35 patients with pain from a phantom limb, traumatic neuroma, or scar tissue. Ultrasonic energy at an intensity of 1 watt per sq. cm. was used with an applicator surface of 5 sq. cm. Treatment lasted 5 minutes daily on 5 or 6 days a week up to a maximum of 12 treatments. Direct mobile treatment with a heavy mineral-oil coupling agent was used in most cases, but if the surface was uneven treatment was given under water with the transducer surface ½ to ¾ inch (12·7 to 19·1 mm.) from the part being treated.

Of the 35 patients treated, 23 were completely relieved of pain, 9 had slight residual pain, and 3 obtained no relief. Five patients whose pain recurred after intervals ranging up to several months were given a second course of treatment with good response. Microscopical examination of tissues from the treated areas was carried out in 5 cases in which subsequent operation was carried out, and showed no evidence of destructive changes in the skin, connective tissue, or nervous tissue.

The authors discuss the various methods which have been used in the treatment of pain of this type and the possible mechanism of its relief by ultrasonic therapy.

J. B. Millard

745. **Biophysical Effects of Ultrasonic Energy on Carcinoma and their Possible Significance**

J. F. LEHMANN and F. H. KRUSEN. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **36**, 452–459, July, 1955. 2 figs., bibliography.

The authors, working at the Mayo Clinic and Foundation, have investigated the effects of ultrasonic energy on Ehrlich's ascitic carcinoma of the mouse grown as a solid tumour of the tail, and on suspensions of cells of the same tumour. A frequency of 1 megacycle per second was used for irradiation, the beam being focused by a polystyrene lens and the focal intensity being 8·4 watts per sq. cm. The apparatus was installed in a steel chamber in which a pressure of 7 atmospheres or a vacuum of 70 cm. of water could be produced. Boiled water was used as the coupling medium. The exposure time for cell suspensions was 1 minute, or 30 minutes at 7 atmospheres pressure, the temperature of the suspension being kept at 20° C. Solid tumours were irradiated for 4 minutes, the body of the mouse during this procedure being kept above the water and therefore not receiving any ultrasonic energy. *X*-ray treatment was given in addition in some experiments.

The destructive effect of ultrasonic energy may be due to the production of cavitation in the tissues by the release of gases, to the rise in temperature resulting from absorption of ultrasonic energy, or to reactions produced by ultrasonic phenomena unconnected with cavitation or thermal effects. In these experiments it was found that when cavitation was prevented by irradiation at a pressure of 7 atmospheres or in a vacuum, and when thermal effects were prevented by cooling, no significant destruction of tumour cells occurred. Ultrasonic irradiation was found to enhance the effect of *x* rays slightly, probably as a result of the thermal effect.

J. B. Millard

746. **The Effect of Repeated Muscular Exertion on Muscle Strength**

H. D. DARCUS and N. SALTER. *Journal of Physiology* [*J. Physiol.* (*Lond.*)] **129**, 325–336, Aug. 29, 1955. 7 figs., 19 refs.

Using a strain-gauge dynamometer to measure isometric force, and a similar apparatus suitably adjusted to measure isotonic power, the authors have compared the effects of isometric and isotonic exercises in developing muscle strength in experiments carried out at the University of Oxford. One group of 6 subjects were required to make a maximum effort against resistance 30 times at 1-minute intervals each day for 5 or 6 consecutive days, the muscular contraction being virtually isometric, while a second group of 6 subjects were required to perform a similar number of isotonic contractions by rotating a spindle against a known resistance. Three members of each group then continued this "training" until 20 to 28 sessions had been completed. The muscles tested were the pronators and supinators of the forearm, and in 2 subjects the elbow flexor muscles. Measurements of isometric force and isotonic work were made before and after each experiment. The effects of motivation were reduced so far as possible by withholding from the subjects the results of each day's tests; in this way they had no accurate indication of the progress that had been made.

Both methods of training produced an increase in muscle strength whether measured isometrically or isotonically, but that produced by isotonic training was the greater and occurred more rapidly. The antagonist muscles and the muscle groups in the opposite limb showed an increase in strength with both training methods.

The authors discuss muscle training, and point out that comparison between the results of different investigators is difficult owing to the use of different techniques and criteria. The importance of lack of interest as affecting the willingness of the subject to exert himself is stressed, and it is suggested that the greater improvement occurring with isotonic training may have been due to the fact that the increase in range of movement could to some extent be assessed by the subject, whereas those performing isometric training had no such index of achievement.

J. B. Millard

Neurology and Neurosurgery

747. **Compression of the Spinal Cord by Extramedullary Neoplasms. A Clinical and Pathologic Study**
H. J. McALHANY and M. G. NETSKY. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath.*] **14**, 276–287, July, 1955. 8 figs., 15 refs.

This report is based on a clinical and anatomic study of 19 cases of extramedullary spinal cord neoplasm. Extramedullary tumors may produce a variety of symptom complexes regardless of their location in the horizontal plane of the spinal canal. Pain usually initiates the syndrome of extramedullary compression, and paraplegia is its usual outcome. The intervening clinical features do not progress in a definite pattern. Thus, urinary tract disturbances may occur early or late in the course, or may not be encountered. Pain is the outstanding symptom, but its absence does not vitiate the diagnosis of an extramedullary tumor. Anatomic study revealed that the anterior columns are less vulnerable to pressure regardless of the location of the tumor in the horizontal plane. Doubt is cast on the importance of the dentate ligaments in spinal cord compression. The pathogenesis of spinal cord compression is believed to be primarily mechanical and secondarily related to the collapse of small intramedullary blood vessels. " Coup " and " contre-coup " effects are the usual result of compression by extramedullary masses. Physical distortion of the spinal cord may also occur and is related to the same mechanism.—[Authors' summary.]

748. **Myasthenia Gravis. Results of Medical Management**
F. R. FERGUSON, E. C. HUTCHINSON, and L. A. LIVERSEDGE. *Lancet* [*Lancet*] **2**, 636–639, Sept. 24, 1955. 3 figs., 10 refs.

This paper presents a follow-up study of 75 cases of myasthenia gravis treated medically at the Manchester Royal Infirmary between 1932 and 1954, the average period of follow-up being more than 10 years and in no case less than 2 years. Six patients could not be traced and 9 had died, 3 of myasthenia and 2 with thymomata; 3 had died of unrelated disorders and in one case no information as to the cause of death was available. All the remaining 60 were re-examined in 1954, when 42 of them were capable of doing what they considered to be full work (this assessment being made independently of the dosage of neostigmine which they were taking). In 44 of the original cases the first symptoms were ocular and in 27 of these the disorder had remained confined to the ocular muscles; in 10 cases other muscles had become involved within the following 2 years, and in 7 at intervals ranging from 3 to 13 years after the initial ocular symptoms. The authors stress the relatively benign nature of myasthenia confined to the ocular muscles; they consider that in assessing clinical progress this group of cases should be separated from those with more generalized myasthenia. The findings in this series give no support to Harvey's suggestion that treatment with neostigmine reduces the frequency and duration of remissions. *J. W. Aldren Turner*

749. **A Benign " Tumour " of the Cerebellum. Report on Two Cases of Diffuse Hypertrophy of the Cerebellar Cortex with a Review of Nine Previously Reported Cases**
D. R. OPPENHEIMER. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **18**, 199–213, Aug., 1955. 20 figs., 11 refs.

An unusual cerebellar abnormality is described in which there is localized enlargement of the folia with the disappearance of the underlying white matter. The tissue, the structure of which is uniform throughout, is formed by a convoluted sheet consisting of two distinct layers—an outer layer continuous with the molecular layer of the normal parts of the cerebellum and containing chiefly nerve fibres, and an inner layer continuous with the granular layer and containing atypical nerve cells. This tissue contains no recognizable granular cells and no Purkinje cells. This abnormality presents as a space-occupying lesion of the posterior fossa; it cannot be classified with any certainty as either a tumour or a malformation.

In the present paper, from the Maida Vale Hospital for Nervous Diseases and the Department of Human Anatomy, Oxford, 2 new cases are described (the patients were males, aged 21 and 52 respectively) and 9 cases from the literature are reviewed. The author suggests that the condition is an unusual form of hypertrophy, rather than a neoplastic growth. *L. Crome*

750. **Prolonged Drainage of the Lateral Ventricles in Neurosurgery.** (Наблюдения над длительным дренажем боковых желудочков мозга в практике нейрохирургической работы)
A. A. ARENDT and S. I. KUZNETSOVA. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] **19**, 3–9, July–Aug., 1955.

The authors began using prolonged drainage of the lateral ventricles in their neurosurgical practice in 1948 and now report their experience in 94 cases, of which 57 were cases of infratentorial tumour, 25 of supratentorial tumour, and 12 of inflammatory lesions. About 70% of the patients were under the age of 16, and the most common tumour encountered was astrocytoma of the cerebellar vermis and hemispheres. Obstructive hydrocephalus was present in all cases and the main purpose of draining the ventricles was as a preparation for radical surgery. Their methods of establishing and maintaining the drainage, the duration of which was usually from 2 to 5 days, are described. The chief dangers of the procedure are injury to the basal ganglia, haemorrhage into the tumour, and infection. The authors discuss the prevention of these complications and also enumerate the precise indications for drainage in the pre- and post-operative periods. *L. Crome*

751. **Treatment of Parkinsonism with a New Compound (B.S. 5930)**
R. O. GILLHESPY and A. HALL RATCLIFFE. *British Medical Journal* [*Brit. med. J.*] 2, 352–355, Aug. 6, 1955. 2 figs.

A new antihistaminic and anticholinergic compound, β-dimethylaminoethyl-2-methylbenzhydryl hydrochloride (B.S. 5930), was tried in the treatment of 73 cases of Parkinsonism at Dudley Road Hospital, Birmingham. The patients were first given inert tablets for 2 weeks; 5 who had improved on previous treatment did not deteriorate when given inert tablets and were therefore eliminated from the trial, together with one patient who had not responded to previous drug treatment but who now improved with inert tablets. Of the remaining 67 patients, 3 had post-encephalitic Parkinsonism, 37 arteriosclerotic Parkinsonism, and 27 the idiopathic form of the disease.

B. S. 5930 was given in a dosage of 50 mg. 3 times a day for 3 or 6 months; in a few cases the daily dosage was 250 mg. At the end of 6 months 43 of the 67 patients had benefited from the treatment, as judged by improvement in tremor, rigidity, and performance of daily tasks. Of 17 patients who had failed to respond to previous treatment with solanaceous alkaloids and benzhexol hydrochloride, 7 improved with B.S. 5930, while of 50 who had responded to previous drug therapy, 14 did not improve with B.S. 5930. The assumption that the improvement in those patients who were better after treatment with B.S. 5930 was indeed due to the drug was proved valid by a further short " double-blind " trial. B.S. 5930 in a dosage of more than 250 mg. daily caused restlessness, blurring of vision, and nausea, but in a dosage of less than 250 mg. daily it caused few side-effects, and no signs of tolerance were observed after 6 months' treatment. It is concluded that B.S. 5930 compares favourably with other drugs in the treatment of Parkinsonism and that it is a most useful addition to those now available. The authors discuss the design of clinical trials of new drugs in Parkinsonism.

[The authors are to be commended for their careful method of evaluating remedies for Parkinsonism.]

Bernard Isaacs

DIAGNOSTIC METHODS

752. **Some Electrophysiological Aspects of Muscular Dystrophy**
F. H. NORRIS and P. O. CHATFIELD. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] 7, 391–397, Aug., 1955. 4 figs., 12 refs.

Electromyograms were recorded at the Clinical Center, National Institutes of Health, Bethesda, Maryland, from the muscles of a number of patients with muscular dystrophy, some with and others without myotonia; the electrodes were fine wires inserted into the muscles with the aid of a hypodermic needle used as a cannula.

Prolonged voluntary contraction in cases of classic progressive muscular dystrophy was sometimes followed by an after-discharge which could not be distinguished from that occurring in the cases of myotonia; further, it might have the characters of fibrillation and could not then be differentiated from the spontaneous activity of denervation.

[The authors are careful not to generalize too widely from these observations. It has, however, become increasingly difficult to maintain the rather sharp distinctions set up only a few years ago between the electrical patterns found in the various neuromuscular disorders.]

William Cobb

753. **The Relation of Age to Metrazol Activated EEGs**
J. FISHER and W. J. FRIEDLANDER. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] 7, 357–361, Aug., 1955. 1 fig., 6 refs.

It has been suggested that a positive electroencephalographic response to " metrazol " (leptazol) is more likely to be found in young than in older subjects. In order to test this assertion, data from about 800 cases collected from 4 published sources were subjected to statistical analysis. While positive results were significantly commoner in young control subjects, there was no support for the view that they were so in patients with convulsive disorders. However, it is stressed that all the patients concerned were over 17 years of age.

William Cobb

754. **A New Method of Activation of the Electroencephalogram: Scalp Electrical Stimulation (SES)**
M. GOZZANO, L. SINISI, G. TONINI, and R. VIZIOLI. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] 7, 407–414, Aug., 1955. 6 figs., 3 refs.

In a number [not specified] of cases of epilepsy and healthy control subjects studied at the Clinic for Nervous and Mental Diseases of the University of Rome stimulation of the scalp with square-wave pulses at 1,000 per second and 20 volts for 30 seconds has been practised during electroencephalography. Changes in the tracing, either local or general, were observed to follow this, in an [again unspecified] proportion of cases of epilepsy in which the findings were abnormal without stimulation, but those with normal tracings and the controls showed no response. It is therefore concluded that pre-existing pathological change is necessary for its development.

It is thought improbable that the stimulus could excite the cortex directly in the given circumstances, so that the effect may be mediated through the meningeal blood vessels.

William Cobb

755. **The Electroencephalogram in Infantile Cerebral Palsy**
M. A. PERLSTEIN, E. L. GIBBS, and F. A. GIBBS. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] 34, 477–496, Aug., 1955. 9 figs., 11 refs.

At the Cook County Hospital (University of Illinois Medical School), Chicago, the electroencephalographic findings in 1,217 cases of cerebral palsy in children under the age of 8 were studied. The patients were divided into three main groups—those with spasticity (68%), those with extrapyramidal lesions (28%), and those with ataxia (4%). Cases of hemiplegia accounted for half of the spastic group. [The authors make the comment

that " although mixed lesions may occur so that spasticity and athetosis coexist, this is the exception; as a rule, spasticity, dyskinesia and ataxia occur as pure syndromes "—a remark with which many clinicians would disagree.] There was a slight preponderance of males except among cases of paraplegia, in which the slight preponderance of females may be related to a high incidence of prematurity, the chance of survival being higher for a female than a male premature infant.

Of the spastic group, excluding cases of paraplegia, 63% had fits, which occurred in only 33% of cases of spastic paraplegia and 22% of cases of athetosis. Grand mal was far more common than petit mal (53% and 2% respectively), whereas 60% of an unselected series of epileptic children had petit mal. Unilateral convulsions were also more common in the cases of cerebral palsy than in the unselected epileptic children, but psychomotor attacks were equally rare in both series (0·4 and 0·5% respectively).

Monopolar recordings, with the patient both awake and asleep, were made in all cases. The tracing was abnormal in 90% of those cases of cerebral palsy with a history of fits and in 44% of those without such a history; as would be expected, abnormal tracings were less common in cases of athetosis. Spikes were found to be the most common abnormality (77%), while wave-and-spike activity was exceedingly uncommon (1%). The spikes were usually focal or asymmetrical; occipital spike foci were common, and often associated with strabismus. There was a tendency for the abnormalities to migrate forwards with increasing age from the occipital to the mid-temporal, and later the parietal and frontal areas. *J. Foley*

756. **An Electroencephalographic Study of Migraine.** (Étude électroencéphalographique des migraines)
R. PANZANI and R. BOYER. *Presse médicale* [*Presse méd.*] **63**, 1211–1214, Sept. 17, 1955. 6 figs., bibliography.

From the Marseilles Faculty of Medicine the authors describe the electroencephalographic (EEG) findings in 110 cases of idiopathic migraine, the records being made in nearly all cases between attacks. In 32 cases the tracing was within normal limits. The 78 abnormal tracings fell into two main groups: (1) 57 showed synchronous bilateral abnormalities, often more marked on the side of the migraine, which in 3 cases constituted a true slow dysrhythmia; (2) 21 records showed focal spike abnormalities of " functional " type.

The literature on this subject is reviewed and the authors attempt to correlate the clinical types of migraine with the EEG findings, suggesting possible pathogenetic mechanisms and considering the relation of migraine to epilepsy. They conclude that when true slow dysrhythmia is present—that is, in the rare " dysrhythmic migraine " first described by Weil (*Electroenceph. clin. Neurophysiol.*, 1952, **4**, 181; *Abstracts of World Medicine*, 1952, **12**, 449)—the angiospastic phenomena may be the result of a primary electrical disturbance in the meso- and di-encephalon and that such cases should be treated with anticonvulsants. The focal EEG abnormalities (which are more common in those cases of migraine accompanied by paraesthesiae and hemiparesis) may, they suggest, be the result of neuronal damage secondary to repeated vasomotor disturbances during attacks of migraine. A further contribution is promised dealing with EEG recordings made during attacks of migraine. *J. B. Stanton*

CEREBRAL VASCULAR DISORDERS

757. **Cortisone in Immediate Therapy of Apoplectic Stroke**
H. I. RUSSEK, A. S. RUSSEK, and B. L. ZOHMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 102–105, Sept. 10, 1955. 18 refs.

In a previous paper (*J. Amer. Geriat. Soc.*, 1954, **2**, 216; *Abstracts of World Medicine*, 1954, **16**, 327) the authors described the striking improvement obtained in 9 out of 12 cases of hemiplegia in response to administration of cortisone within 48 hours of the onset of symptoms. Because of these encouraging results they decided to give this treatment in all cases of acute hemiplegia due to cerebral thrombosis or embolism coming under their care, and in this paper they report results in 35 such cases. Hypertension was present in 24 of the patients, and a history of angina pectoris was obtained in 8 and of previous myocardial infarction in 7. Cortisone was given by mouth in a dosage of 300 mg. daily for the first 2 days, this dosage being progressively reduced thereafter to a maintenance dose of 50 mg. daily in the third week. In 21 of the patients there was " striking clinical improvement " within 24 hours, and in 27 there was " remarkable neurological recovery " by the end of the third week. No significant untoward side-effects of cortisone were observed. *P. D. Bedford*

758. **Hemiplegia Caused by Cerebrovascular Thrombosis. An Arteriographic Study**
K. E. LIVINGSTON, A. ESCOBAR, and G. D. NICHOLS. *Journal of Neurosurgery* [*J. Neurosurg.*] **12**, 336–344, July, 1955. 7 figs., 23 refs.

The authors state that cerebrovascular thrombosis has not been systematically studied by means of carotid angiography and that " a majority of reports in the literature pertaining to thrombosis affecting the cerebral circulation are concerned with occlusions of the internal carotid artery proximal to the cerebral vessels ". While they agree that internal carotid thrombosis is undoubtedly more frequent than was previously suspected, they consider that " it is probable that the hemiplegic syndrome clinically considered secondary to thrombosis results more commonly from occlusion of the cerebral portion of the circulation ". In this paper they describe the angiographic findings in 30 patients with hemiplegic " stroke ", all having histories and clinical findings typical of cerebrovascular thrombosis involving the cortical motor system. The patients' ages ranged from 23 to 85 years, one-third being over 60. In patients showing obvious clinical improvement arteriography was avoided, those studied including only patients in whom the neurological picture had become stabilized or was

deteriorating. No ill effects from percutaneous carotid angiography with 35% diodone were observed.

The angiograms in 18 of the 30 cases showed well-defined vascular obstruction, which in 8 cases was "extracerebral", involving the internal carotid artery at or distal to the bifurcation of the common carotid in the neck in 7, and the distal portion of the carotid siphon intracranially in one. In 10 cases the obstruction was distal to the siphon. In the remaining 12 cases the arteriographic appearances were "within normal limits".

Failure to demonstrate vascular occlusion in such a large proportion (40%) of cases may be attributable to inability to visualize the finer vascular bed or to recognize subtle but critical changes in the vascular pattern. However, the appearance of a "normal" vascular pattern in spite of marked loss of function is not inconsistent with experimental observations that transient occlusion of the middle cerebral artery frequently results in a persistent hemiparesis, even though blood flow subsequently appears to be fully re-established. In this series the potential for recovery appeared to be greater in patients with "normal" arteriographic findings than in those in whom a major occlusion was demonstrable.

The authors mention two possible sources of error in diagnosis: (1) patients who have no occlusion demonstrable by carotid arteriography may later prove to have occlusion in the vertebral–basilar arterial system; (2) patients in whom definite occlusion is demonstrated may subsequently prove to have an infiltrating tumour of the hemisphere although there was no significant displacement of vessels at the time of arteriography.

[Most clinicians in Great Britain avoid performing arteriography in unselected cases of hemiplegia thought to be due to vascular occlusion, in the belief that it is dangerous, particularly in elderly hypertensive patients. The authors do not state whether their 30 patients were selected from a much larger number of cases of hemiplegia, but the fairly high incidence of internal carotid occlusion found suggests that they were, and their findings conform to those usually encountered in Britain.]

J. MacD. Holmes

759. Arterenol (Norepinephrine) and Vascular Headache of the Migraine Type. Studies on Headache

A. M. OSTFELD and H. G. WOLFF. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **74**, 131–136, Aug., 1955. 6 figs., 13 refs.

In this article from the New York Hospital–Cornell Medical Center the authors describe observations on the effects of "arterenol" (noradrenaline) on the intensity and duration of migrainous headache and postulate a theory of causation of the headache.

An intravenous infusion of one litre of 5% dextrose solution containing 4 ml. of 0·2% solution of noradrenaline was given on 116 occasions to 35 patients during an attack of migraine at a rate sufficient to increase the systolic blood pressure by 10 to 40 mm. Hg. At regular intervals the blood pressure and pulse rate were recorded and the deep-pain threshold of the scalp measured in terms of the pressure required to elicit pain; when possible the diameter of dilated cranial vessels was also measured, and observations made of accompanying phenomena such as oedema, conjunctival injection, and rhinorrhoea. At the same time the patients' reports on changes in intensity of the headache were recorded.

On 93 of the 116 occasions the headache began to diminish within 10 to 60 minutes of starting the infusion and was much reduced or eliminated in 20 to 160 minutes. In 4 cases of status hemicranicus the infusion had no significant effect. In one case of ophthalmoplegic migraine the diplopia disappeared and ocular movements returned to normal 70 minutes after starting the infusion, whereas in previous attacks weakness of the 6th nerve had persisted for 4 days. Another patient with ptosis of the right eyelid, usually lasting 48 hours, recovered normal lid movement 90 minutes after the beginning of the infusion. In 4 patients with moderately severe essential hypertension vascular headaches were similarly terminated on 7 occasions, the optimum effect being obtained by giving the infusion at a rate which caused an average rise in blood pressure of 28/9 mm. Hg. No serious or permanent ill-effects of arterenol administration were noted. The authors also found that whereas diminution of the deep-pain threshold in the skin of the scalp persisted for hours or days after the spontaneous termination of an attack of migraine, it returned rapidly to normal if the attack was terminated by giving noradrenaline or ergotamine tartrate.

Upon the basis of these and other observations it is postulated that at the onset of a migrainous headache the dilatation of cranial arteries and arterioles raises the hydrostatic pressure in the capillaries and thus promotes the escape into the tissues of increased amounts of a "deep-pain threshold lowering substance", and that pain results from the dilatation of large arteries and the accumulation of this substance in the tissues. Administration of noradrenaline constricts the arteries and arterioles and reduces capillary hydrostatic pressure, thus allowing speedy reabsorption of the "pain substance" and relieving the pain. *Marcel Malden*

760. Headache and Hydration. The Significance of Two Varieties of Fluid Accumulation in Patients with Vascular Headache of the Migraine Type

A. M. OSTFELD, D. J. REIS, H. GOODELL, and H. G. WOLFF. *Archives of Internal Medicine* [*Arch. intern. Med.*] **96**, 142–152, Aug., 1955. 7 figs., 8 refs.

Two kinds of oedema have been observed in association with migraine: (1) a localized accumulation of fluid in those areas of the scalp where headache is experienced, associated with tenderness and variable "pitting"; (2) a more generalized fluid retention developing before the onset of headache and demonstrable by a gain in weight and by pitting of dependent parts of the body. At the New York Hospital–Cornell Medical Center these two types of oedema have been studied by various methods.

Before and during an attack of migraine the bulbar conjunctival vessels were examined by an ophthalmic slit-lamp. Vasodilatation was almost constant during an attack, with evidence of oedema and sometimes haemorrhage; less constantly vasoconstriction preceded

the attack. After intravenous injection of diluted noradrenaline vasoconstriction occurred with clearing of local oedema. The small bulbar conjunctival vessels were found to be more sensitive at the onset of an attack of headache to local application of noradrenaline, and sensitivity was greatly reduced during the attack. Local oedema during an attack of migraine was accompanied by local vasodilatation; this was associated with a lowering of deep pain thresholds, and the evidence suggests that in the local fluid accumulation there are substances which damage tissue, lower the pain threshold, and make the dilatation of large arteries more painful.

The non-localized oedema was not always coincident with the headache, and often appeared during periods of increased alertness and activity. It could be induced in patients subject to migraine without also inducing headache and could be abolished without preventing headache. It was thus neither causally nor mechanically related to the mechanism of the headache.

Hugh Garland

CEREBRAL INFECTIONS

761. **The Treatment of Purulent Meningitis.** (Le traitement des méningites suppurées)
C. Chorémis, J. Nicopoulos, C. Tsenghi, and N. Matsaniotis. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **12**, 148–157, 1955. 27 refs.

The authors review the results in 364 cases of purulent meningitis in young children treated at the University Medical Clinic, Athens, between January, 1950, and June, 1954. In the first period (1950–2) of 164 patients treated with sulphonamides and penicillin by both the intramuscular and intraspinal routes, 140 recovered and 24 died. In the second period (1952–4) of 200 patients treated with the same drugs but by intramuscular administration alone, 186 survived and only 14 died. In both groups a significant proportion of the patients were admitted to hospital *in extremis*. The authors record their conviction that intrathecal treatment is unnecessary and possibly harmful.

[The methods employed and results achieved do not differ in any noteworthy way from those in other published series.] *M. E. MacGregor*

762. **The Surgical Treatment of Cysticercosis of the Fourth Ventricle with Special Features of its Postoperative Course.** (О хирургическом лечении цистицеркоза IV желудочка и особенностях послеоперационного течения)
N. Y. Vasin. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] **19**, 28–35, July–Aug., 1955. 2 figs., 4 refs.

The author analyses the results in 33 cases of cysticercosis of the 4th ventricle treated by operation at the Burdenko Institute of Neurosurgery, Moscow. In some of these cases the lesions were more widespread, but in all of them the operation was undertaken either on account of imminent or already present obstruction of the cerebrospinal fluid in the aqueduct, or because of involvement of structures situated in the floor of the ventricle. In the first 11 operations access was gained by large posterior decompression, but after 1944 (22 operations) a much smaller area, with a median incision giving access through the squamous portion of the occipital bone, was found to be adequate. Details of the operation and postoperative course are discussed. Of the 33 patients, 4 died at, or within a few days of, the operation, but the others survived, and some have been followed up for varying periods up to 16 years. Of these, 50% showed complete recovery; some, however, had symptoms of meningeal inflammation, while others showed gradual deterioration of varying degree down to complete helplessness or death. *L. Crome*

763. **The Morbid Anatomy and Clinical Features of Multiple Metastatic Abscesses of the Brain.** (К патоморфологии и клинике множественных метастатических абсцессов головного мозга)
D. G. Zhuchenko. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] **19**, 35–43, July–Aug., 1955. 2 figs.

In 30 out of 90 cases of metastatic brain abscess seen at the Burdenko Institute of Neurosurgery, Moscow, there were multiple foci of suppuration, and in 17 of these secondary brain abscesses had developed as the result of local spread. The brains of these patients were studied histologically, large sections being made through both hemispheres. It was found that these secondary and subsequent abscesses showed increasing irregularity, such as imperfection in the arrangement of the wall, and that these irregular features were reflected clinically in the severity of symptoms and signs, which were more marked than those produced by the primary and more regularly formed lesions. The possible value of this observation in the clinical detection of multiple abscesses and their location is discussed. *L. Crome*

764. **A Peculiar Form of Encephalomyelitis.** (О своеобразной форме энцефаломиэлита)
A. N. Shapoval and E. S. Sarmanova. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 75–80, No. 9, Sept., 1955. 1 ref.

The authors report the observation of 26 cases of an unusual type of encephalomyelitis in which the onset was acute and accompanied by pyrexia, headache, vertigo, rigors, nausea, and vomiting. In some cases clouding of consciousness supervened, with somnolence and diplopia; paresis and other focal signs also developed, but in some instances these were delayed until after the temperature had come down and been normal for several weeks. The 26 patients described came under observation because of neurological sequelae 3 to 15 years after the acute stage of the disease; in 5 cases the neurological involvement was progressive and the disease took the form of a chronic infection. The main residual symptoms were weakness of the limbs, pain in the back, lowered motor activity, mental retardation, monotonous speech or dysarthria, and emotional lability; 2 patients showed post-infective psychosis, and 5 some limitation of movement of the spine with slight kyphosis. In some cases there was limitation of the field of vision, and other ocular conditions observed were chorioretinitis, ptosis, strabismus, anisocoria, reduced reaction to light, loss of

accommodation, nystagmus, depression of corneal reflexes, and facial, glossopharyngeal, vagal, and hypoglossal nerve palsies. Some patients were left with tri- or quadri-plegia, the paralysis being spastic in type, with exaggerated and unequal tendon reflexes, dysdiadochokinesis, and incoordination.

The results of tests for antibodies to 10 known types of encephalitis virus were entirely negative. An infective agent was isolated by means of intracerebral inoculation of mice with blood and cerebrospinal fluid from 5 patients in the chronic stage of the disease. The type of encephalomyelitis described was localized in a particular geographical area of the U.S.S.R., and inquiry showed that a disease of similar type had been known in this region for many years. The authors propose that the disease be called " Vilyui encephalomyelitis ", from its place of origin. *D. J. Bauer*

CEREBRAL TRAUMA

765. **Signs of Obstruction of the Superior Longitudinal Sinus following Closed Head Injuries (Traumatic Hydrocephalus)**
J. P. MARTIN. *British Medical Journal* [*Brit. med. J.*] 2, 467–470, Aug. 20, 1955. 9 refs.

The author reports a series of 5 cases in which head injury was followed by symptoms and signs of raised intracranial pressure. In each case there was an interval, varying from 2 days to 3 weeks or more in duration, before these symptoms and signs became apparent. Abnormal signs other than papilloedema developed in 4 of the cases —paresis of the sixth nerve in 2, disturbance of upward eye movement in one, weakness of both sides of the body in one, and an extensor plantar response in one case. Epileptic fits occurred in 2 cases. In none of them was there evidence of any localized intracranial space-occupying lesion. Ventriculography was performed in one case only and the appearances were normal. Angiography was not performed in any case. Lumbar puncture was carried out in 2 cases, the pressure being raised in one and normal in the other. In all cases recovery ensued without operative interference. Treatment in individual cases is not detailed, but the author states that some were treated with magnesium sulphate by rectum and mouth. In no case was repeated lumbar drainage or temporal decompression performed, nor were anticoagulants used, though it is suggested that this last measure might be useful in some cases.

The author believes that the appearance of raised intracranial pressure after a head injury and without evidence of a localized thrombosis is strongly suggestive of partial or complete obstruction of an intracranial venous sinus—sometimes the lateral, sometimes the superior longitudinal sinus—and he applies this diagnosis to his cases. He feels that the presence of partial paralysis of legs and arms with sparing of the hands and face is confirmatory evidence and indicates the spread of clotting to the superficial cortical veins. He compares this syndrome with " otitic hydrocephalus ", which he believes to be due to the same cause.

[It is important to note that in none of these cases was sinus obstruction demonstrated either at post-mortem examination or by angiography. Investigation of " otitic hydrocephalus " by angiography usually fails to demonstrate sinus obstruction, and in the absence of such positive evidence it would seem advisable to withhold anticoagulant therapy.] *Brodie Hughes*

EPILEPSY

766. **Epilepsy and Chronic Tetany.** (Epilepsie et tétanie chroniques)
H. P. KLOTZ. *Revue neurologique* [*Rev. neurol.* (*Paris*)] 92, 254–269, 1955. 4 figs., 14 refs.

In this paper from the Hôpital Bichat, Paris, the author describes a form of epilepsy arising in patients who show signs of chronic tetany in the absence of any disturbance of blood calcium or potassium levels or of alkalosis.

Of 68 such cases of normocalcaemic tetany, clinical and electroencephalographic signs of epilepsy were found in 12. The resemblance of the epilepsy in these cases to that occurring in hypocalcaemic tetany is pointed out, together with the fact that some of the patients also suffered from cataract. Treatment with vitamin D_2 or dihydrotachysterol was found to suppress the epilepsy completely in 4 and partially in 8 of 16 cases, even when the usual anticonvulsants had been of no avail. A significant feature was the resistance of these patients to the hypercalcaemia normally resulting from prolonged administration of vitamin D_2. Moreover, even when this treatment proved beneficial, clinical signs of chronic tetany (such as Chvostek's sign) often persisted, and could also be found unaccompanied by epilepsy in the patients' relatives. *J. B. Stanton*

767. **Studies of the Mechanism of Stimulus-sensitive Myoclonus in Man**
C. W. WATSON and D. DENNY-BROWN. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] 7, 341–356, Aug., 1955. 9 figs., 19 refs.

The clinical and electrographic findings in a patient suffering from myoclonus epilepsy, said to be of the Unverricht–Lundborg type and to be due to cerebral lipoidosis, are reported from Boston City Hospital (Harvard Medical School). Stimuli of various kinds gave rise to appropriately located cerebral responses and to restricted myoclonic jerks, both electrical and muscular responses becoming more generalized with repetition of the stimulus and culminating in convulsions. As others have noted previously, the relation between cortical discharge and myoclonus in this type of case may not be a constant one.

It is postulated [without it appearing to follow from the evidence provided by this case] that myoclonus is due to a breakdown of a diffuse character in synaptic resistance, which might be due to distension of neurones, to loss of cells with consequent instability, or to a biochemical factor. *William Cobb*

768. **The Electroencephalogram of Psychomotor Seizures in Childhood**
G. H. GLASER and L. M. GOLUB. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] 7, 329–340, Aug., 1955. 5 figs., 28 refs.

In the considerable volume of recent work on psychomotor epilepsy little attention has been paid to the effects of age on the electroencephalogram. Accordingly, the authors examined the tracings of 110 children between 1½ and 16 years of age who were considered to have this form of attack. The findings were normal in 37 cases, temporal spikes were present in 12, bilateral 3-c.p.s. spike-and-wave forms in 14, bilateral 1½–3-c.p.s. spike-and-wave forms in 20, and other abnormalities in 27. On examination of tracings made during sleep 4 more cases with temporal spikes were found, but the spike-and-wave forms of abnormality were reduced in 14 cases.

This is a very different state of affairs from that found in adults, and the authors discuss various mechanisms involving the temporal and limbic cortex and the thalamoreticular systems which might explain it.

[To the abstracter the predominance of spike-and-wave patterns seems only to follow the well-known age-distribution trends, and the whole analysis to emphasize the inadequacy of "psychomotor epilepsy" as a useful diagnostic concept.] *William Cobb*

769. **A New Treatment of Status Epilepticus. Intravenous Injections of a Local Anesthetic (Lidocaine)**
C. G. BERNHARD, E. BOHM, and S. HÖJEBERG. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] 74, 208–214, Aug., 1955. 7 refs.

This paper from the Karolinska Institute and the Serafimerlasarett, Stockholm, describes the anticonvulsive effects of lignocaine (lidocaine, "xylocaine") on prolonged epileptic convulsions in 10 cases. In 6 status epilepticus occurred after an intracranial operation, in one after a severe head injury, and in one after air encephalography. The remaining 2 cases were of the idiopathic type. Lignocaine was given by intravenous infusion in a concentration of 1 or 2% in dextrose or saline solution, the dose being 1 to 6 mg. per kg. body weight per hour, or by intermittent intravenous injection in doses of 0·6 to 6 mg. per kg. In severe cases the two methods were combined. No untoward effects were noted.

In 2 cases of grand mal and 2 cases of prolonged Jacksonian convulsions attacks were terminated by a single intravenous injection of lignocaine. In 3 cases of status epilepticus administration of lignocaine by infusion was alone sufficient to arrest the convulsions, while in 3 similar but more severe cases the infusion had to be supplemented by repeated intravenous injections. In these cases it was also found possible markedly to increase the anticonvulsive properties of lignocaine by the intravenous administration of barbiturates in doses insufficient in themselves to control the fits, and this synergism has since been confirmed in experiments on animals. As only a very small dose of barbiturate is needed, the ill effects of its sedative action are avoided. The authors suggest the use of this combination of drugs in postoperative cases of status epilepticus, as it would not mask the appearance of signs due to intracranial bleeding.

The details of the clinical state and effects of treatment with lignocaine in each of the 10 cases are described in detail. *Marcel Malden*

770. **The Hyperkinetic Syndrome in Epileptic Children**
C. OUNSTED. *Lancet* [*Lancet*] 2, 303–311, Aug. 13, 1955. 1 fig., 21 refs.

A clinical and sociological study of 70 hyperkinetic epileptic children is reported, the children representing 8% of a large unselected series with epilepsy and convulsive disorders in three general hospitals at Oxford, Swindon, and Northampton respectively. The features of the hyperkinetic syndrome, which are described, included a peculiar attraction to running water and euphoria, the latter sometimes giving a paradoxical response to small doses of dexamphetamine sulphate. The syndrome usually evolved from a primary cerebral injury within the first 5 years of life, and was more common in males than females. The cerebral injuries ranged from birth trauma (18 cases) to status epilepticus as a result of "cryptogenic" epilepsy, most types of seizure being observed except those of pure petit mal. The electroencephalographic findings, the effects of anticonvulsant drugs and of dexamphetamine, as well as the parental reactions and the management of these cases are described. The nature of the hyperkinetic syndrome is discussed in terms of a defect in attention, and it is suggested that "a simple clinical analysis can be employed to measure the characteristics of the syndrome." *J. B. Stanton*

771. **Chlorpromazine (Thorazine) Treatment of Disturbed Epileptic Patients. Preliminary Report**
V. I. BONAFEDE. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] 74, 158–162, Aug., 1955.

From a total of 2,300 epileptic patients in a New York State colony, 78 of the most actively disturbed were chosen for a study of the effects of chlorpromazine on behaviour in such cases. The patients were all females, their ages varying from 12 to 61; 27 were suffering from symptomatic and 51 from idiopathic epilepsy. In many cases the epilepsy was fairly well controlled by anticonvulsants, psychic and motor disturbances constituting the major problem of management in all. Most of the patients were mentally defective and some were frankly psychotic. Chlorpromazine was given initially by intramuscular injection in doses of 100 mg. or by mouth in doses of 200 to 300 mg. daily, the amount being decreased or increased subsequently as necessary. In order to determine the effect of the drug on the epileptic state of the patients, they were divided into three groups, in one of which the usual dosage of anticonvulsants was continued, while in the second group it was reduced by one-third, and in the third group by one-half.

In 6 cases of acute excitement chlorpromazine given by injection was effective within 30 to 45 minutes, the patients becoming quieter and more relaxed. It was

considered to be "far superior" to scopolamine, apomorphine, and the barbiturates previously used. In chronically disturbed behaviour states the effect of chlorpromazine was also favourable, the behaviour in 41% of cases being "markedly", in 25·6% "moderately", and in 16·7% "slightly" improved, while only 13 patients remained unimproved. The improvement consisted in decreased noisiness, aggressiveness, and destructiveness, and a reduced need for sedatives or ancilliary measures. In 56 cases the patient gained weight during chlorpromazine therapy. Some increase in the frequency of seizures occurred, but was almost exclusively confined to the two groups in which the dosage of anticonvulsants was reduced, and control was re-established with its return to the previous level.

Reversible coma occurred in one case, and in another chlorpromazine may have contributed to occurrence of fatal status epilepticus. Other complications included macular or maculo-papular rashes, constipation, and in 2 cases jaundice with clay-coloured stools, which disappeared 6 days after chlorpromazine was discontinued.

Marcel Malden

CEREBRAL TUMOURS

772. **Meningiomas of the Posterior Fossa. Their Diagnosis, Clinical Features, and Surgical Treatment**
J. W. MARKHAM, C. A. FAGER, G. HORRAX, and J. L. POPPEN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **74**, 163–170, Aug., 1955. 5 refs.

Meningiomata within the posterior fossa differ widely in mode of onset and in symptomatology and often cause difficulty in diagnosis. The literature up to 1954 contains only five reports of significant numbers of cases, and the present authors therefore record their experience in 29 cases treated surgically at the Lahey Clinic, Boston, between January, 1934, and December, 1953. The cerebellopontine angle was the most frequent site of the tumour. Headache, tinnitus, an unsteady gait, and loss of hearing were the most frequent subjective symptoms, while impaired hearing, hypalgesia or hypaesthesia of the face, absent or decreased corneal reflex, and facial weakness were the commonest cranial nerve signs. Supratentorial extension of some degree occurred in 8 cases. The tumour and capsule were completely removed in 22 cases, and partially removed in 7. Of the 29 patients, 7 died in the immediate postoperative period, 13 survived more than 5 years, and 9 for more than 10 years. It is of interest that 2 patients subjected to incomplete removal survived 12 and 14½ years respectively. The authors state that in some instances incomplete removal may be a necessary procedure to avoid serious damage to the cranial nerves or brain stem.

The symptomatology most commonly simulated was that of acoustic neurinoma. Over the whole series the average duration of symptoms before operation was 3·6 years, the longest period being 11 years and the shortest 5 weeks. In 13 (out of 24) cases the radiographs did not reveal any significant abnormality, but in 5 of the remainder there was erosion or thinning of the internal auditory meatus or medial end of the petrous ridge, and in 3 dense calcifications in the posterior fossa were seen. Negative radiographs appeared to be of little value in excluding the presence of these tumours. Ventriculography was performed in 13 cases: in 5 the fourth ventricle was partially demonstrated and was seen to be displaced from its anatomical position, so that more precise location of the tumour was possible before operation; in 2 cases the ventriculogram suggested an occipital or parieto-occipital tumour

J. MacD. Holmes

773. **The Specific Diagnosis of Meningioma from the Vascular Pattern (with Special Reference to Serial Angiography).** (Die Artdiagnose des Meningeoms im Gefässbild (unter besonderer Berücksichtigung der Serienangiographie))
W. SCHIEFER, W. TÖNNIS, and G. UDVARHELYI. *Deutsche Zeitschrift für Nervenheilkunde* [*Dtsch. Z. Nervenheilk.*] **172**, 436–456, 1955. 6 figs., 41 refs.

The conclusions reported in this paper are based on the arteriographic investigation at the University Neurosurgical Clinic, Cologne, of 150 cases of meningioma, in 114 cases by simple arteriography only and in 36 by serial angiography, the latter procedure demonstrating not only the first, arterial, phase but also the subsequent venous and post-venous phases of angiography.

The authors state that even simple arteriography may show the displacement of the normal vessels which is typical of meningioma; it also reveals the blood supply of the tumour, showing whether this is derived from the internal or external carotid. Frequently the suspicion that a meningioma is present is confirmed by the presence of "marginal" vessels on the arteriogram.

In only 14 (12·2%) of the 114 cases examined by simple arteriography was there opacification of the tumour by the contrast medium, whereas this occurred in 14 (38·8%) of the 36 cases investigated by serial arteriography. The type of meningioma could not be diagnosed from the arteriographic picture, but its presence was usually indicated by a general slowing down of the cerebral circulation. It was found that opacification of the tumour begins in the middle of the arterial phase, becoming most pronounced in the venous phase, and occasionally may persist even beyond that phase. These circulatory peculiarities are typical of meningiomata and are caused by a slowing down of the blood circulation in the specific vascular systems of these tumours.

There was failure of opacification of the tumour in 57% of the 150 cases investigated, although in about one-quarter of these the diagnosis of meningioma was suggested by the presence of "marginal" vessels. Among the 66 cases showing only a non-specific displacement of the larger vessels there were 11 cases of olfactory meningioma and 27 of meningioma of the cribriform plate, the diagnosis in these cases being based on the location of the tumour and the typical vascular displacement. In only 28 out of the 150 cases investigated could no opinion on the nature of the tumour be advanced after the performance of arteriography.

A. Orley

Psychiatry

774. **Adrenochrome as the Cause of Schizophrenia: Investigation of Some Deductions from this Hypothesis**
A. J. LEA. *Journal of Mental Science* [*J. ment. Sci.*] **101**, 538–547, July, 1955 [received Sept., 1955]. 21 refs.

Accepting as a working hypothesis the suggestion of Hoffer, Osmond, and Smythies (*J. ment. Sci.*, 1954, **100**, 29; *Abstracts of World Medicine*, 1954, **16** 240) that adrenochrome or some related metabolite is a cause of schizophrenia, the author has made a number of deductions. Three of these—relating (1) to the use in the treatment of schizophrenia of sodium chloride and ascorbic acid to inhibit adrenaline oxidation, (2) to treatment by reducing dietary intake of tyrosine and phenylalanine as in phenylpyruvic amentia, and (3) to the likelihood that excess or abnormal indole bodies are present in the urine of schizophrenics—are merely stated. Two further hypotheses—relating to abnormal pigmentation and to negative association with allergic states—are fully investigated. With regard to the first, it is postulated that, as tyrosine is a precursor of melanin as well as of adrenaline, and as the unstable adrenochrome is easily oxidized to melanin, schizophrenics may overproduce melanin. In this connexion it was found from Service and recruiting-board records that dark-haired individuals were significantly more common among schizophrenics than among a control series of patients with injury, but only in the age group 15 to 19. As regards the second hypothesis, the author postulates that, as schizophrenics are reported to show an increased tolerance to histamine, and as adrenaline and adrenochrome antagonize histamine, allergic states should be of low incidence in schizophrenics. Support for this hypothesis was obtained from a comparison of the case records of schizophrenics and of patients with head injury. The implications of both these findings are discussed at length. The author considers that his findings are consistent with the further hypothesis that adrenochrome intoxication, and hence schizophrenia, is related to hepatic dysfunction, both hereditary and acquired. *A. C. Tait*

775. **The Hyperventilation Syndrome**
F. AMES. *Journal of Mental Science* [*J. ment. Sci.*] **101**, 466–525, July, 1955 [received Sept., 1955]. 19 figs., bibliography.

This paper contains a full discussion of the physiological and psychiatric aspects of the hyperventilation syndrome, here regarded as a stress reaction having its origin in the inability of modern man, inhibited by cultural and social traditions of behaviour, to apply the classic " fight or flight " solution.

After a historical review of the literature the author gives a detailed account of the protean symptomatology of hyperventilation, including sections on electroencephalographic and electrocardiographic signs, based on 40 cases seen at the Groote Schuur Hospital, Cape Town, which are described in detail. Three separate physiological mechanisms appear to be invoked: an increased alkalinity of the blood, a reflex peripheral vasoconstriction, and circulatory effects resulting from the muscular exercise of overbreathing; adrenaline release during stress may enhance or maintain these three responses. In the 40 cases described respiratory complaints were rarely pronounced, and the respiratory difficulty was never exactly contemporaneous with exertion. Some of the cases had been misdiagnosed as of unspecified neurosis, epilepsy, hypoglycaemia, thyrotoxicosis, peripheral vascular disease, poliomyelitis, organic and functional cardiac disease, tetany, or acroparaesthesia. In diagnosis demonstration of symptoms by voluntary hyperventilation is stressed. This is also said to be useful therapeutically, as also are discussion, re-education, and relaxation and breathing exercises.

Much original experimental work on the peripheral vasoconstrictor effect of hyperventilation, investigated by plethysmographic methods, is also described. In both clinical cases and controls pulse volume, digital volume, and arterial inflow were reduced by overbreathing, but patients with hyperventilation tended to suffer originally from cold hands and to be more responsive to reflex vasoconstriction. Cooling and elevation of the limbs accelerated the onset of paraesthesiae and sympathectomy delayed it and diminished its intensity. Thus it is postulated that ischaemia from peripheral vasoconstriction, as well as alkalosis, contributes to the excitation of the peripheral nerves. *A. C. Tait*

776. **Neurosis in General Practice**
J. C. E. POUGHER. *British Medical Journal* [*Brit. med. J.*] **2**, 409–412, Aug. 13, 1955. 6 refs.

The author analyses the incidence of neurotic symptoms in 500 consecutive patients (273 females and 227 males) who came for consultation in a general practice in Leamington Spa (population 38,000), and discusses the causes, symptomatology, and treatment. The diagnosis of functional illness was based on: (*a*) atypical nature of the symptoms; (*b*) presence of anxiety or apprehension towards the symptoms or—as in hysteria—apparent indifference; (*c*) tendency to dramatize or exaggerate symptoms; and (*d*) past history. Evidence of neurosis was found in 50 males and 131 females (36·2%). It was estimated during the survey that in one month 47·6% of all consultations were sought by patients with some form of neurosis.

Incidence in terms of age and sex is tabulated [but not corrected for age-grouping in the town population]; 50% of the males and 57% of the females were over 50 years. A total of 172 symptoms were elicited from males (3·4 per patient) and 512 from females (3·9 per patient). These symptoms are tabulated, but only a

very wide classification was possible. The five most frequent symptoms in males were abdominal pain, depression, headaches, tiredness, and chest pain; and in females headache, depression, tiredness, abdominal pain, and insomnia.

The 181 cases were divided into two groups: (1) those in which the emotional adjustment broke down under stress; and (2) those in which there appeared to have been only partial adjustment since childhood. In Group 1 there were 33 males and 94 females, and the four commonest precipitating factors were: in males, ill-health, fear of ill-health, occupational stress, and marital problems; and in females marital problems, inability to deal with domestic stress, insecurity of old age, and fear of ill health. In Group 2 there were 17 males and 37 females, and these presented the most difficult problems, since improvement was possible only by adjustment to a way of life.

Treatment, which is discussed, included firm reassurance, adequate physical examination, regular but controlled visits, but no placebos (the author states that none of the 172 patients observed for a year sought medical advice elsewhere). The results in these 172 patients after one year were: "apparent cure", 92; "greatly improved", 36; "some improvement", 27; "no change", 17. *John C. Kenna*

TREATMENT

777. Electrical Treatment of Anxiety States

J. D. MONTAGU and L. S. DAVIES. *Journal of Mental Science* [*J. ment. Sci.*] **101**, 577–592, July, 1955 [received Sept., 1955]. 19 refs.

The authors, who consider that, in general, reports on the therapeutic use of subconvulsive electrostimulation in anxiety states are unconvincing, have conducted a trial of this treatment in order to "provide an unbiased evaluation". The subjects of the investigation were 100 patients admitted to the Roffey Park Rehabilitation Centre, Horsham, Sussex, and the stimulation was by brief, unidirectional "square waves". Of the first 50 patients, 25 were treated by stimulation at 500 pulses per second, and of the second 50 patients 25 received stimulation at 200 pulses per second, the remaining 25 patients in each group serving as controls. Pains in each group were matched on the basis of type of anxiety state, criteria for which are given. Thiopentone anaesthesia was induced in treated patients and controls, and the procedure was imitated in the latter up to the point of induction. An average of 12 treatments were given to each individual, accompanied by ordinary psychotherapy but not by electrically stimulated abreactions. A "blind assessor" examined the patients clinically before and after treatment and again 3 months later. Psychometric tests and Funkenstein's test were also applied before and after treatment.

The clinical results showed no evidence that this therapy enhanced the response of the treated patients. The results of the psychometric tests showed a significant association with the clinical findings; but whereas the reaction to adrenaline in Funkenstein's test was significantly associated with the clinical findings in patients who had adrenaline-precipitable anxiety, this was not considered to be prognostically valuable.

[Apart from its immediate interest, the method of this careful trial merits much consideration.] *A. C. Tait*

778. Prolonged Sleep Treatment in Mental Disorders (Some New Psychopharmacological Considerations)

H. AZIMA. *Journal of Mental Science* [*J. ment. Sci.*] **101**, 593–603, July, 1955 [received Sept., 1955]. 36 refs.

The author, from McGill University and the Allan Memorial Institute of Psychiatry, Montreal, describes experiments in prolonged sleep therapy of mental disorders with a combination of chlorpromazine and different time-reacting barbiturates. The subjects studied were 25 patients with various psychiatric disorders who had failed to respond to other therapeutic measures. Treatment, the technique of which is described, was given for an average period of 25 days, and patients were followed up for at least 12 months. Improvement is claimed in 15 of the 25 cases. The results are discussed in detail, and this is followed by a critical examination of neurophysiological and psychological theories of sleep and sleep treatment. The author's own "organodynamic" theory postulates a changed relation between self-sustaining functional neuronal systems and the nonspecific central reticular activating system whereby, broadly, inhibition of the latter is inferred to facilitate gratification, exhaustion, and reintegration of the former. Finally indications for sleep therapy are discussed. The author rightly stresses the relative neglect of this method of treatment in Anglo-American psychiatry, and suggests further therapeutic approaches. *A. C. Tait*

779. Liver Function and Hepatic Complications in Patients Receiving Chlorpromazine

I. M. COHEN and J. D. ARCHER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 99–101, Sept. 10, 1955. 2 refs.

Jaundice developed in 5 out of over 800 patients receiving chlorpromazine therapy at the University of Texas. The jaundice, which proved to be benign, was of the obstructive type and was thought to be due to individual drug idiosyncrasy. In all the cases the icterus disappeared on withdrawal of the drug and the usual symptomatic treatment. In 84 patients the effect of chlorpromazine on liver function was assessed from the quantitative van den Bergh reaction, the serum alkaline-phosphatase and cholesterol levels, urinary excretion of bilirubin and urobilinogen, cephalin–cholesterol flocculation, thymol turbidity, serum total protein level with albumin–globulin ratio, prothrombin time, and "bromsulphalein" retention. The maximum daily dosage of chlorpromazine varied from 100 to 1,000 mg., and the average duration of treatment one month (range 1 week to 5 months). No significant change in hepatic function, as revealed by these tests, was observed, and the authors conclude that under ordinary conditions chlorpromazine is not toxic to the liver. *H. B. Stoner*

Dermatology

780. **Atrophie Blanche en Plaque**
L. M. NELSON. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] **72**, 242–251, Sept., 1955. 12 figs., 21 refs.

Atrophie blanche en plaque is a sclerotic change in the skin usually occurring on the inner side of the lower leg near the malleolus. There are telangiectases and often small painful and tender ulcers. The change may be primary or may follow vesicular, bullous, or haemorrhagic lesions, or these may occur in the course of the disease. Sometimes the condition is seen in conjunction with varicose veins and their complications, especially in middle-aged women, and is probably of vascular origin. In this paper the literature is reviewed and 6 cases observed personally by the author are presented.

Among conditions most likely to be mistaken for atrophie blanche en plaque is the painful type of ulceration described by Corlette as irritable ulcer of the malleolus, both diseases tending to occur in middle-aged women with impaired circulation. The condition also has features in common with hypertensive ischaemic ulceration, though in the latter the ulcers are usually larger. There is no distinctive histology by which atrophie blanche may be recognized. The epidermis is thinned and flattened and overlies a sclerotic, thickened dermis, with little cellular infiltration; some change in the vessels is present and there is some formation of new capillaries.

Treatment is not discussed, but healing is said to be slow. *John T. Ingram*

781. **Exudative Diffuse and Papular Dermatosis Developed after Discontinuation of ACTH and Cortisone. Treatment of Eczematous Skin Diseases**
P. H. NEXMAND. *Danish Medical Bulletin* [*Dan. med. Bull.*] **2**, 97–100, July, 1955. 1 fig., 11 refs.

Although patients with chronic eczematous skin diseases may benefit from treatment with ACTH or cortisone, when this is discontinued there may be recurrence or exacerbation of the original skin condition or even the development of new symptoms. The author has observed this sequence of events in 4 cases treated at Rigshospitalet, Copenhagen, and describes 2 of them. He considers that the new condition which sometimes follows withdrawal of hormone therapy in such cases is a clinical entity. Certain features are characteristic. A diffuse exudative and papular dermatosis appears symmetrically on the extremities and sometimes on the face, the skin being red and infiltrated with lymphocytes and plasma cells. The affected areas are well demarcated and mask the original condition. They are resistant to treatment except by repetition of ACTH or cortisone therapy, on withdrawal of which the eruption reappears, sometimes with greater intensity than before. He concludes that in chronic eczematous conditions hormone therapy should be used only with the greatest caution. *S. T. Anning*

782. **The Tzanck Test.** (Der Tzanck-Test)
R. HAENSCH. *Hautarzt* [*Hautarzt*] **6**, 407–409, Sept., 1955. 4 figs., 18 refs.

In 1947 Tzanck described a cytological method for the diagnosis of pemphigus vulgaris, in which material taken from the base of the vesicles is air-dried on slides and stained by Pappenheim's method. In pemphigus vulgaris a uniform picture of rounded cells with dark nuclei and many large nucleoli is found. These cells come from the Malphigian layer and can be separated from each other, as the intercellular bridges have disappeared.

These findings were confirmed by the present author at the Municipal Skin Clinic, Wuppertal-Elberfeld, Germany, in 12 patients with pemphigus vulgaris, and were in striking contrast to those in similar preparations made from 12 patients with dermatitis herpetiformis. Here the presence of lymphocytes and neutrophil and eosinophil granulocytes made the picture much more polymorphic and the uniform appearance of pemphigus vulgaris was never seen. Preparations from a number of other vesicular eruptions were similarly examined and could always be distinguished from pemphigus vulgaris. The method is simple, quick, and apparently specific for the diagnosis of pemphigus vulgaris. *G. W. Csonka*

783. **Use of Hydrocortisone and 9-*alpha*-Fluorohydrocortisone Derivatives. Evaluation in the Treatment of the Pruritic Dermatoses**
I. I. LUBOWE. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] **72**, 164–170, Aug., 1955. 6 figs., 14 refs.

From experience at the Metropolitan and the Flower and Fifth Avenue Hospitals, New York, the author has found that hydrocortisone in a 1% ointment or a 2·5% lotion is effective in relieving pruritus and reducing inflammation in atopic dermatitis, neurodermatitis, dermatitis venenata, and anogenital dermatitis. He has also found that 9-α-fluorohydrocortisone in a 0·1% ointment or a 0·25% lotion is as effective in these conditions as the hydrocortisone preparations. The results obtained with the two ointments were, however, slightly better than those obtained with the lotions. When neomycin or bacitracin was added to the ointment, excellent results were achieved in lichen simplex chronicus, nummular eczema, and secondarily infected allergic dermatoses. Sensitization with these preparations was rare. The author states that the dermatoses often relapse when treatment ceases completely, but that application of lotion or ointment once a day will usually prevent such a relapse. Long-continued maintenance therapy is not advisable, however, when ulcerative or vesicular lesions are present. It is suggested that the incorporation of hydrocortisone compounds in standard skin medicaments " may reduce the index of sensitization of these compounds ". *E. Lipman Cohen*

784. **Standard Patch Tests in Eczema and Dermatitis**
H. T. H. WILSON. *British Journal of Dermatology* [*Brit. J. Derm.*] 67, 291–298, Aug.–Sept., 1955. 2 figs., 10 refs.

Multiple patch tests on the skin, read after 48 hours, were performed on three groups of 50 patients with, respectively, contact dermatitis, discoid eczema, and atopic eczema, and on 50 controls. The test substances were: (1) 5% nickel sulphate in water; (2) 10% sodium arsenate in water; (3) 5% ammoniated mercury in soft paraffin; (4) 0·5% potassium dichromate in water; (5) 2% procaine hydrochloride in water; (6) 6% formalin in water; (7) 50% potassium iodide in soft paraffin; (8) 1% *para*-phenylene diamine in soft paraffin; (9) 50% oil of turpentine in olive oil; and (10) tincture of pyrethrum. There were thus 500 individual tests in each group, 34 (6·8%) of which gave a positive reaction in the control groups, 75 (15%) in the group with atopic eczema, 70 (14%) in the group with discoid eczema, and 118 (23·7%) in the group with contact dermatitis.

When 6 of the patients with contact dermatitis were later retested with the same and greater dilutions of the substances which had given a positive reaction the results were again positive with all dilutions. When 8 of the patients with atopic eczema were similarly retested, of 19 tests, 9 gave a negative, 9 showed an irritant, and one a " non-specific " false positive reaction. None of the 19 reactions conformed to the allergic pattern. It is considered that patients with contact dermatitis are polysensitive and that many of the positive reactions obtained, therefore, are false. *R. R. Willcox*

785. **A New Antifungal Antibiotic Mycostatin (Nystatin), for the Treatment of Moniliasis: a Preliminary Report**
M. B. SLOANE. *Journal of Investigative Dermatology* [*J. invest. Derm.*] 24, 569–571, June, 1955. 8 refs.

The author reports, from Columbia University College of Physicians and Surgeons, New York, the treatment of 8 cases of moniliasis of the skin and mucous membranes with " mycostatin " (" nystatin "; fungistatin). This was administered in the following forms: troches, each containing 3,000 units; an ointment of 50,000 units per g. in an oleaginous base; a vaginal suppository containing 30,000 units; and a freshly made solution in propylene glycol containing 150,000 units per ml. There was a prompt clinical response, which was confirmed by laboratory studies, but a tendency to relapse when the antibiotic was stopped. *E. W. Prosser Thomas*

786. **Pigmented Nevi. A Clinical Appraisal in the Light of Present-day Histopathologic Concepts**
B. SHAFFER. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] 72, 120–132, Aug., 1955. 3 figs., 7 refs.

The macroscopic characters of 204 pigmented naevi were studied before removal in an attempt to find features which could be used to forecast the histology. Solid nodular lesions (135; classified as polypoid 4, sessile 14, dome-shaped 107, and papillary 10) were almost without exception clearly benign. Slightly elevated flat lesions (9) and verrucous growths (flat lesions with " fine digitate excrescences ") (26) were nearly all compound naevi. Lesions with a halo showed junctional activity. Flat macular lesions were either junctional naevi or inactive lentigines; in cases of junctional naevi the patients were younger and the pigmentation was often irregular.

The author considers that with these criteria the presence of junctional activity can be forecast on clinical grounds with a high degree of accuracy. Some interesting observations on the relation of the various clinical types to age and site are presented.

Bernard Lennox

787. **The Effect of " Colcemid " on Cutaneous Epitheliomata.** (Considerazioni sull'effetto del colcemid negli epiteliomi cutanei)
A. AGOSTINI. *Archivio italiano di dermatologia, sifilografia e venereologia* [*Arch. ital. Derm.*] 27, 271–281, 1955. 9 figs., 7 refs.

The experimental investigation of the antimitotic properties of colchicine is hampered by its toxicity. However, its desacetylmethyl derivative " colcemid " is stated to be 20 to 40 times less toxic and equally effective; it has been used with success in the treatment of leukaemia and with doubtful benefit by local application to cutaneous epitheliomata.

The author has treated 14 cases of epithelioma at the Institute of Clinical Dermatology of the University of Bologna by the infiltration into and around the tumour of 1 to 2 ml. of colcemid solution (1 mg. per ml.) repeated every 3 or 4 days to a total of 7 to 10 doses. There were 10 cases of epithelioma of the face and 2 of the hand, one case of Bowen's disease in the shoulder region, and one case of vulval epithelioma. The infiltration is painful, but less so than with oestrogens and the pain rapidly passes off. There were no local or general side-effects necessitating interruption of the treatment. In 3 cases there appeared to be a clinical cure after follow-up for 2 to 3 months. In 4 cases the lesion became smaller and in 6 it remained unchanged, while the vulval lesion deteriorated after the treatment. Biopsy was carried out before and after treatment in all cases.

The process of cure starts with a violent necrotic reaction, followed by shrinkage of the whole lesion—possibly due to fibrosis—and then re-epithelization, leaving a slightly depressed scar of atrophic appearance. Histological examination, even in cases of apparent clinical cure, shows a reduced and damaged, but not completely destroyed, tumour; there is disruption and separation of the tumour cells, diminished staining, and a decrease in the size of tumour-cell groups, which seem to lie in empty spaces. Nuclear changes are prominent, consisting in pyknosis or pykno-necrosis, swelling or ballooning of the nucleus, the chromatin being scattered in small clumps, or compression of the nucleus with cystic dilatation of the rest of the cell; these changes are often present simultaneously. There is no characteristic reaction in the connective tissue surrounding the tumour. In tumours not responding to the treatment similar changes are seen, but on a smaller scale. On the whole the effect of intradermal infiltration of epitheliomata with colcemid is variable and unpredictable.

F. Hillman

Paediatrics

788. **Observations on Weight Gain in Infants**
J. THOMSON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 322–327, Aug., 1955. 4 figs., 14 refs.

Gain in weight at 4-weekly intervals during the first year of life was recorded for infants born at the Simpson Memorial Maternity Pavilion and Royal Infirmary, Edinburgh, a total of 1,737 observations being made on male and 1,605 on female offspring of first pregnancies whose birth weight was within the range 5½ lb. to 9½ lb. (2·5 to 4·3 kg.). There was no significant difference between the mean birth weight of males and that of females, but the mean gain in weight of boys at 52 weeks exceeded that of girls by 22 oz. (624 g.). No statistically significant association was observed between birth weight and subsequent gain in weight. Almost invariably infants of low birth weight gained weight more rapidly than did those whose birth weight was higher. The author did not find any support for the view that infants double and treble their birth weight at certain ages.

Comparison of the infant weights reported by Paton and Findlay (*Spec. Rep. Ser. med. Res. Coun.* (*Lond.*), 1926, No. 101) with those observed in the present investigation revealed an increase in the mean body weight of male and female infants of the order of 2 lb. (0·9 kg.). It is suggested that the weight-graph cards used in many local authority infant welfare centres are largely outmoded, that the usual method of recording infant weight should be abandoned, and that only gains and losses from birth should be recorded.

Marianna Clark

INFANT FEEDING

789. **Clinical and Chemical Studies in Human Lactation. X. The Maintenance of Breast-feeding**
F. E. HYTTEN and A. M. THOMSON. *British Medical Journal* [*Brit. med. J.*] **2**, 232–237, July 23, 1955. 6 figs., 21 refs.

The authors have investigated the incidence of successful breast-feeding, that is, its maintenance up to at least the 3rd month of life as the sole source of the infant's diet, by examining the health visitors' records for 2,404 single legitimate babies born in the City of Aberdeen in 1951 out of a total of 2,769, of whom 76% were born in Aberdeen Maternity Hospital, 7% in a private nursing home, and 17% at home.

At 3 months the proportion of all the infants fully breast-fed was 35·6%, the proportions in those born in a private nursing home, hospital, and at home being 44·5, 35·6, and 32·4% respectively. At 6 months the proportions of infants still being breast-fed, although receiving supplementary food, in the 3 groups were 28·8, 25·7, and 20·2% respectively. It was shown that at 3 months the older mothers were more likely to be breast-feeding (39% of women over 30 years), while the reverse was the case at 10 days in hospital-delivered patients. Infants of second pregnancies showed a higher incidence of breast-feeding at 3 months than those of first pregnancies. Correlation with the Registrar-General's social classes showed the following incidence of breast-feeding at 3 months: 50% in Classes I and II, 36% in Class III, and 31% in Classes IV and V. It was noted that Classes I and II had the lowest incidence during the first week post partum, but this was probably owing to the higher average maternal age and the larger proportion of primigravidae. Another observation was that taller women of better physique were more likely to be still breast-feeding at 3 months (42%) compared with smaller women (31%).

The authors calculate that on the basis of the baby's requirements being one litre of milk per day at 4 months (providing 50 Cal. per lb. (110 Cal. per kg.) body weight) and the efficiency of conversion of energy intake into milk energy about 60% the moderately active lactating mother's requirements must average 3,200 Cal. per day, allowing only 2,100 Cal. for her own maintenance. It is reasonable to suppose that the healthy woman in good economic circumstances is more likely to take such a diet. (Further research is contemplated to establish the relative contribution to breast-feeding of the various factors involved.)

Elaine M. Osborne

790. **Feeding Difficulties in Infancy. Their Cause and Prevention**
U. JAMES and B. L. COLES. *British Medical Journal* [*Brit. med. J.*] **2**, 656–658, Sept. 10, 1955. 10 refs.

To determine the factors responsible for the feeding problems for which children are admitted to the Violet Melchett Mothercraft Home, London, the case histories of 173 infants entering the Home during the year from October, 1953, were studied. Of these infants 62 were breast-fed, 83 artificially fed, and 28 were mixed feeders; 30 were premature. In the breast-fed group most of the difficulties occurred in firstborn children, and the authors believe that the mothers had not been adequately instructed. Maternal age was not obviously related to the incidence of feeding difficulties. It was noted that the social conditions of the homes of breast-fed infants were better than those of the artificially fed.

[The findings are incompletely analysed and all the conclusions are not necessarily valid in relation to these findings.] In the authors' view most feeding problems can be avoided by: (1) adequate instruction of the mother; (2) proper antenatal care of the breasts; (3) a better knowledge of the caloric value and composition of infant foods in order to avoid underfeeding; (4) avoidance of frequent change from one type of infant food to another; and (5) introduction at an early age of mixed feeding.

Kathleen M. Lawther

PREMATURITY AND NEONATAL DISORDERS

791. The Clinical and Pathologic Aspects of Premature Perinatal Death

G. W. ANDERSON and R. E. L. NESBITT. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **97**, 113–135, Aug., 1955. 4 figs., 20 refs.

Premature perinatal deaths occurring at Johns Hopkins Hospital, Baltimore, between January, 1937, and December, 1949, were analysed in an attempt to determine the nature of the pathological changes and the specific cause of death. During the period under review there were 26,776 births, 3,008 of which were premature; although these premature births represented only 11·2% of the total, deaths of premature infants (566) accounted for 54% of the total infant mortality. Of these 566 deaths, 253 (44%) occurred before birth, 177 of them (31%) before the onset of labour. At necropsy a specific pathological cause for death was found in only 67 of these 177 cases, anoxia due to abruptio placentae being the most frequent. Of the 76 deaths occurring during labour (13% of all deaths of premature infants), 65 were due to a specific aetiological factor, anoxia (45 cases) again being the commonest, followed by cord obstruction and abnormal labour. In the group of 313 premature infants dying after birth the principal causes of death were associated with anoxia (70 cases); the "largest single entity" was, however, deficient pulmonary ventilation, hyaline membrane being present in many of the cases.

Factors responsible for the production of premature labour are discussed, the authors concluding that "advancement in the science of muscle chemistry and physiology appears to be the principal hope in the ultimate solution of this problem". *David Morris*

792. Respiratory Capacity in the Neonatal Period

S. ENGEL. *Lancet* [*Lancet*] **2**, 266–267, Aug. 6, 1955. 2 refs.

The newborn infant is kept near the danger zone of respiratory insufficiency because of the volume of dead space in the lung and the anatomical impossibility of taking a deep breath. The volume of each individual breath (tidal air) is about 20 c.cm., necessitating frequent inspiration to supply the oxygen required. The total lung volume averages 120 c.cm. The author calculates that the bronchial tree and the blood vessels (of approximately equal calibre) occupy about 30% of the infant's lung volume, compared with 10 to 15% in the adult. The horizontal ribs and relatively large liver limit inspiratory expansion of the chest. To compensate for this, the width of the trachea (5 to 6 mm.) is much greater in relation to total lung volume in the infant than in the adult (15 mm. with a lung volume of 3,000 c.cm.). If the width of the adult's trachea were in the same proportion to lung volume as in the infant it would be 15 cm. across. Moreover, the individual acinus of the infant's lung is smaller than that of the adult's, giving a larger respiratory surface per unit volume; yet even so the respiratory surface per kg. body weight is only one-third of that of the adult. These limitations should be remembered in the management of the newborn. *A. White Franklin*

793. Concentration of Bilirubin in Cerebrospinal Fluid in Hemolytic Disease of the Newborn

R. STEMPFEL and R. ZETTERSTRÖM. *Pediatrics* [*Pediatrics*] **16**, 184–195, Aug., 1955. 5 figs., 22 refs.

The bilirubin content of the cerebrospinal fluid (C.S.F.) of 23 infants born to Rh-immunized mothers was estimated at Karolinska Sjukhuset, Stockholm, on 51 occasions and compared with that of the serum. All 23 infants were Rh-positive and gave a positive reaction to the Coombs test; although 13 of them were so badly affected as to require exchange transfusion (which had to be repeated in 3 cases), there were also a number who were only mildly affected.

No direct correlation was found between the serum and C.S.F. bilirubin levels, which suggests that the permeability of the blood–brain barrier is subject to individual variations. Estimations of the total protein content of the C.S.F. were also made, the values being found generally to be high compared with a mean level of 103·35 mg. per 100 ml. in 14 normal newborn infants; the protein and bilirubin levels in the C.S.F. showed a high correlation. Generally where there was marked indirect hyperbilirubinaemia the bilirubin in the C.S.F. was predominantly of the indirect-reacting type. The pattern of the bile pigments in one case of "physiological jaundice" showed no difference from that found in the cases of haemolytic disease. *John Murray*

CLINICAL PAEDIATRICS

794. Fat Absorption Studies in the Diagnosis and Treatment of Pancreatic Fibrosis

C. A. C. ROSS. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 316–321, Aug., 1955. 1 fig., 12 refs.

An investigation was carried out at the University of Birmingham "to ascertain the magnitude of the fat absorption defect in pancreatic fibrosis by means of fat-balance studies and chylomicrographs, and to compare the findings with those obtained in coeliac disease. From the fat-absorption findings in pancreatic fibrosis an attempt was made to estimate the value of pancreatin in treatment and to place dosage on a rational basis". The subjects of the study were 22 children with pancreatic fibrosis and 18 with coeliac disease at the Children's Hospital, Birmingham, all the patients being under 5 years of age.

In children between one and 5 years of age fat absorption was always less than 60% in pancreatic fibrosis, and always more than 60% in coeliac disease. In those less than one year old no such difference was found. The chylomicron counts were carried out under standardized conditions both in the fasting state and also after a meal containing 5 to 20 g. of fat, depending on age. It was found that the maximum chylomicron increment was, on an average, lower in children with pancreatic

fibrosis than in those with coeliac disease. In the children with pancreatic fibrosis the administration of pancreatin resulted in an average increase in fat absorption of 23%, a rough correlation being found between the optimal dosage of pancreatin and the age of the patient. *H. Harris*

795. **The Correlation of Clinical and Bacteriological Findings in Infantile Gastro-enteritis**
R. McLaren Todd and E. G. Hall. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 345–353, Aug., 1955. 8 refs.

In this paper from the Alder Hey Children's Hospital, Liverpool, an investigation is reported of the clinical and bacteriological findings and the response to chloramphenicol, aureomycin, and sulphadiazine in 215 cases of infantile gastro-enteritis seen over a recent 2-year period. On admission rectal swabs were taken and examined with special reference to the presence of certain serologically identifiable strains of *Escherichia coli*. Those cases in which *E. coli* Type O111 or Type O55 was isolated were classified as " positive ", the remainder, including cases in which other serologically identifiable strains of *E. coli* might have been present, being classified as " negative ". Patients with *Salmonella* or *Shigella* infection were excluded from the investigation.

The patients were divided into two groups, one, a control group, receiving " routine " treatment without drugs, the other the routine treatment plus chloramphenicol, or aureomycin, or sulphadiazine. Usually, symptoms were more severe in infants in the positive group than in those in the negative group. In the latter chloramphenicol had little influence on the course of the illness, whether mild or severe. It had a mild suppressive action on the total *E. coli* flora and a marked suppressive effect on the two specific *E. coli* types. This was reflected in the finding that in the negative group the rate of recovery of those receiving routine treatment only did not differ significantly from that of patients given chloramphenicol, whereas in the positive group patients given chloramphenicol recovered in about half the time taken by those given routine treatment only. The clinical and bacteriological findings were similar in the small number of patients treated with aureomycin or sulphadiazine. *Marianna Clark*

796. **Epidemic Diarrhea among Infants Associated with the Isolation of a New Serotype of *Escherichia coli*: *E. coli* O127:B8**
M. L. Cooper, E. W. Walters, H. M. Keller, J. M. Sutherland, and H. J. Wiseman. *Pediatrics* [*Pediatrics*] **16**, 215–227, Aug., 1955. 47 refs.

During an outbreak of epidemic diarrhoea at the Children's Hospital, Cincinnati, rectal swabs from 145 infants, 115 of whom had diarrhoea at some time during their stay in hospital, and from 82 adult hospital personnel were cultured, 395 cultures being made from swabs from the children and 149 from the adults. Swabs from 44 of the children and one nurse gave positive cultures for a new serotype of *Escherichia coli*, designated O127:B8. Of the 44 children, 42 were in the first year of life and 20 were in the first month. Clinically, the diarrhoea associated with this serotype was characterized by sudden extreme abdominal distension in some infants, explosive onset, and the presence of a peculiar pungent, musty, objectionable odour.

Neomycin was given by mouth in 36 of the 44 cases with a positive culture in doses ranging from 6 to 80 mg. per kg. body weight daily for 2 to 26 days (mean 8 days). Of 22 patients with positive cultures, *E. coli* O127:B8 was still present after the termination of neomycin treatment in 12, although only 2 had a recurrence of diarrhoea. Administration to every infant in the wards affected of 40 to 50 mg. of neomycin per kg. daily was followed by a decrease in the incidence of diarrhoea and in the detection of *E. coli* O127:B8 in swab cultures. This dosage of neomycin appeared to be of definite therapeutic and prophylactic value, although not bacteriologically adequate. Four of the infants whose rectal swabs yielded a positive culture of this serotype died, and necropsy showed haemorrhagic enteritis in 3. One death from severe diarrhoea occurred among the children with negative cultures. Examination of sera from patients and personnel failed to show the presence of agglutinins for *E. coli* O127:B8. Tests *in vitro* showed the organism to be sensitive to the following antibiotics, in decreasing order of effectiveness: polymyxin, neomycin, chloramphenicol, tetracycline, and oxytetracycline. *E. H. Johnson*

797. **Treatment of Intussusception in Children. A Brief Survey Based on 1,838 Danish Cases. (I. 1,042 Cases 1928–1935. II. 796 Cases 1944–1949)**
J. Munck Nordentoft and H. Hansen. *Surgery* [*Surgery*] **38**, 311–319, Aug., 1955. 21 refs.

In this report from the Aalborg County Hospital and the University of Aarhus, Denmark, the treatment of intussusception in children by the barium-enema technique is evaluated on the basis of: (I) 1,042 cases which were treated in the years 1928–35, and (II) 796 cases treated during 1944–9, collected from a number of Danish hospitals.

In Series I conservative therapy (including barium-enema reduction) was used in 584 cases (56·5%) and primary operation in 450 cases (43·5%); 7 cases did not receive any treatment. In Series II primary operation was employed in only 74 cases (9%), the barium-enema technique in 715 cases (91%), and 7 cases had no treatment. The total mortality in Series I was 19·4%, and in Series II 9·2%. Analysis of the mortality in relation to the duration of symptoms showed that for Series I the death rate for cases treated within 24 hours of the onset of symptoms was 11·7%, compared with 38·5% if treatment was delayed longer than 24 hours. The corresponding figures for Series II were 3·1% and 26·4%. It is noted that over the period investigated the proportion of successful reductions by the barium-enema technique rose from 49% (Series I) to 58% (Series II). Finally it is stressed that in Denmark " surgical measures are required only if this method [barium-enema reduction] fails or if the result is questionable ". *I. McLean Baird*

798. **Treatment of Ascariasis in Children with Piperazine Adipate**

M. HANNA and A. H. SHEHATA. *British Medical Journal* [*Brit. med. J.*] 2, 417–418, Aug. 13, 1955. 11 refs.

From a review of the literature on the treatment of ascariasis in man the authors have noted that there are disadvantages in respect of instability and side-effects attaching to the use of piperazine hydrate, citrate, and diphenylacetate. Piperazine adipate, on the other hand, appears to be an effective, stable, and non-toxic agent for the treatment of oxyuris infestation. They therefore used the last-mentioned drug to treat 85 children (from 1½ to 12 years of age) with ascaris infestation at the Children's Hospital, Mounira, Cairo. [For details of dosage and duration of treatment the original should be consulted.] Complete blood, urine, and stool examinations were carried out before and after treatment.

From the results it appears that piperazine adipate is a safe and effective drug for the treatment of ascariasis in children. The dosage recommended is 0·75 g. for each year of life up to 6 years of age, and 4·5 g. for 6 years and upwards, to be given for one day in 4 equal doses at 4-hourly intervals, after meals. No toxic effects or side-reactions were noted, and the tablets were not objected to by the children. *Kathleen M. Lawther*

799. **A Surgical Treatment Proposed for Either Endocardial Fibroelastosis or Anomalous Left Coronary Artery**

R. N. PAUL and S. G. ROBBINS. *Pediatrics* [*Pediatrics*] 16, 147–165, Aug., 1955. 8 figs., 22 refs.

In both endocardial fibroelastosis and anomalous left coronary artery (in the latter condition the vessel arises from the base of the pulmonary artery) the end-result is ischaemia of the myocardium of the left ventricle with, usually, death from cardiac failure in early infancy. The authors of this paper from the John Gaston and Le Bonheur Children's Hospitals, Memphis, Tennessee, first discuss the clinical features of these two conditions and then describe a new surgical approach. It is emphasized that the differential diagnosis may not be possible except by retrograde aortography, which is not without risk in infants and may be a failure. The only way of achieving improvement in these otherwise hopeless conditions lies in producing an effective collateral circulation to the myocardium, and exact differential diagnosis is not, therefore, essential.

Poudrage of the pericardium with talc, which is the simplest method of revascularizing the myocardium, and has been shown to be effective in adults with myocardial ischaemia, was carried out in 4 infants under one year. An anterior thoracotomy was performed through the 4th left intercostal space, the 4th and 5th costal cartilages being divided. The pericardium was opened widely, pericardial fluid aspirated, and about 5 g. of sterile powdered talc (*U.S.P.*) placed evenly over the surface of the left ventricle and, to a lesser extent, over the anterior surface of the right ventricle. The pericardium was sutured, a small opening being left for the escape of fluid, and the pleural cavity drained. Of the 4 infants, 3 survived approximately one year with clinical improvement. In one of the survivors the diagnosis of anomalous left coronary artery was suggested by a history of "anginal attacks" and electrocardiograms suggestive of anterior infarction; in the other 2 the clinical diagnosis was fibroelastosis. The remaining patient with fibroelastosis died from cardiac failure 4 days after operation.

It is emphasized that this is only an interim report and that further follow-up is essential before the results of the operation can be properly assessed.

F. J. Sambrook Gowar

800. **Anaphylactoid Purpura (Schönlein–Henoch Syndrome). A Long-term Follow-up Study with Special Reference to Renal Involvement**

R. J. P. WEDGWOOD and M. H. KLAUS. *Pediatrics* [*Pediatrics*] 16, 196–206, Aug., 1955. 9 figs., 19 refs.

Between 1936 and 1953 36 children were admitted to the Babies' and Children's Hospital (Western Reserve University), Cleveland, Ohio, with anaphylactoid purpura, of whom 26 were re-examined in 1954. All 26 were considered "well"; at onset their ages ranged from 1 to 12½ years, but most were between 2 and 4, and there were twice as many males as females. No specific antigen was implicated in any case. All children had purpura on the lower limbs, with further spread in 13 cases. Urticaria, erythema, oedema, and small macules or papules were also present; 16 children had joint swelling, 11 had abdominal pain, and 7 melaena. Blood examination showed striking abnormalities. Proteinuria was present in 9 cases, and microscopic haematuria in 6, with hypertension in 4 of these.

When re-examined, in most cases 2 or more years after the onset of the disease, the acute stage had abated in all 26 children. Urinary abnormalities, characterized by haematuria and casts rather than by proteinuria, were found in 10 cases, being present in 9 of the 13 children over 6 years old at onset, and one of the 13 under that age. The sex difference seen in the attack rate was not evident in respect of the degree of renal involvement. The occurrence of urinary abnormality in the acute stage was related to some extent to subsequent renal involvement.

It is suggested that the 10 children in whose urine abnormalities were found were suffering from a "latent nephritis", and that a mild or unnoticed attack of anaphylactoid purpura in childhood might be the origin of unexplained chronic nephritis in adult life in some cases. *E. H. Johnson*

801. **Intramuscular Oxytetracycline: Its Use in Penicillin-resistant Acute Respiratory Infections in Pediatrics**

E. J. DENENHOLZ, F. L. ROBINSON, and W. E. FORNEY. *Antibiotic Medicine* [*Antibiot. Med.*] 1, 453–465, Aug., 1955. 24 refs.

The authors describe their experience in the treatment of respiratory infections by the intramuscular injection of oxytetracycline in 249 infants and children, 212 being treated in private practice and 37 at the Stanilaus County Hospital, Modesto, California. The patients ranged in age from 1 month to 9 years, and the majority were suffering from acute tonsillitis or tracheo-bronchitis.

The indication for the use of oxytetracycline in these cases was the failure of treatment with aqueous procaine penicillin in daily doses of 200,000 to 600,000 units for 1 to 3 days to exert a demonstrably beneficial effect.

Oxytetracycline was diluted to a concentration of 50 mg. per ml. with sterile water or saline, the diluted solution also containing 50 mg. of magnesium chloride per ml. and 2% procaine hydrochloride. The dosage used in domiciliary practice varied, according to age, from 1·4 mg. to 10 mg. per lb. (3 to 22 mg. per kg.) body weight given once in 24 hours. In hospital the dosage was 6 to 20 mg. per lb. (13·2 to 44 mg. per kg.) daily, 2 to 16 injections being given at intervals of 6 or 12 hours, the course lasting 2 to 5 days. Treatment was then continued by mouth when necessary in a dosage of 10 mg. per lb. (22 mg. per kg.) daily in 3 or 4 doses for 4 to 8 days. Local reactions occurred in 6 cases, redness and induration developing at the injection site Oxytetracycline appeared to cause more pain on injection than did penicillin.

A good response was considered to have occurred only when the oral temperature fell to normal or the rectal temperature to below 100° F. (37·8° C.) within 24 hours. Of the 249 cases treated, the response was good in 134 and indefinite in 21, while in 94 there was no response.

The authors conclude that a dose of 3 to 5 mg. of oxytetracycline per lb. (6·6 to 11 mg. per kg.) given once daily is suitable both at home and in hospital, adding a rider [which will be echoed in Great Britain] that greater frequency of injection is not easily practicable in the former case.

[The authors' intention of proving the value of intramuscular oxytetracycline in the treatment of penicillin-resistant respiratory infections cannot be said to have been carried out in this trial. In particular, real evidence of penicillin resistance in any of the cases treated was absent. In the abstracter's view there is no justification for the parenteral administration of any antibiotic in the management of minor infections in children.]

I. M. Librach

802. **The Hypothyroid Infant and Child. Therapy with Sodium L-Thyroxine**

D. A. FISHER, G. D. HAMMOND, and D. E. PICKERING. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **90**, 6–21, July, 1955. 9 figs., bibliography.

The diagnosis, prognosis, and treatment of infants and children suffering from hypothyroidism are discussed in relation to 12 representative patients seen at the University of California Medical Center, San Francisco. Investigations included psychometric and radiological examinations, estimation of the uptake of radioactive iodine before and after administration of thyroid stimulating hormone, and determination of the serum protein-bound iodine and butyl-extractable iodine levels. Of the 12 patients, 6 were under 4 years of age and the condition had been present for periods varying from 5 to 21 months; in 4 of these cases respiratory distress was a striking early sign. In all the patients the serum level of protein-bound iodine was below 4 μg. per 100 ml. and skeletal age was below chronological age; hypercholesterolaemia was present in only one case. Mental retardation was noted in 5 patients and was not materially affected by treatment, although this proved adequate for relief of other clinical features; the mental development was normal in the 6 older patients who developed hypothyroidism after the age of 4 years.

All 12 patients responded satisfactorily to treatment with sodium L-thyroxine and no toxic effects were observed. The dosage employed was related to the needs of the individual, and ranged from 0·2 mg. daily for an infant weighing 20 lb. (9 kg.) to 0·3 mg. daily for a child of 60 lb. (27·2 kg.). The serum protein-bound iodine level was a valuable guide to therapy, satisfactory results being obtained when the level was over 6 μg. and below 12 μg. per 100 ml. Determination of bone maturation and skeletal age were also helpful in assessing thyroxine dosage.

Animal experimental work suggests that the thyroxine requirements of certain tissues, such as liver, muscles, and skin, are less than those of the central nervous system and bone. Thyroxine intake should clearly be sufficient for the needs of all tissues, and it is especially important in the early years of life that the needs of the central nervous system should be satisfied. *R. M. Todd*

803. **Delayed Speech and Developmental Aphasia**

M. MORLEY, D. COURT, H. MILLER, and R. F. GARSIDE. *British Medical Journal* [*Brit. med. J.*] **2**, 463–467, Aug. 20, 1955. 1 fig., 5 refs.

In this paper from the Royal Victoria Infirmary and the Medical School, King's College, Newcastle upon Tyne, the authors give an analysis of speech difficulties, based on 278 cases of delayed speech in children seen over the past 6 years, and using a classification previously suggested by two of them (*Proc. roy. Soc. Med.*, 1950, **43**, 579). The roles of mental retardation, partial or severe deafness, crossed laterality, and social and familial factors are discussed. The authors emphasize that delayed development of the use of language is a manifestation of delayed neurological development, so that determined efforts to teach the child to speak will be ineffective and are likely to be positively harmful.

[The " Burst scale " in this paper is, presumably, the " Burt scale ".] *R. S. Illingworth*

804. **Infantile Spastic Hemiplegia. II. Laterality of Involvement**

P. N. HOOD and M. A. PERLSTEIN. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **34**, 457–466, Aug., 1955. 12 refs.

Left and right infantile spastic hemiplegics have been compared with respect to the rate of language and motor development, intelligence, and birth weight. In contradistinction to previous reports in the literature no significant differences were found between the two groups, except for a greater incidence of right hemiplegics and a heavier mean birth weight for right hemiplegics.—[Authors' summary.]

See also Allergy, Abstract 650.

Public Health

805. **Evaluation of the 1954 Poliomyelitis Vaccine Field Trial. Further Studies of Results Determining the Effectiveness of Poliomyelitis Vaccine (Salk) in Preventing Paralytic Poliomyelitis**

T. FRANCIS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 1266–1270, Aug. 6, 1955.

The author summarizes the results of further examination by the Vaccine Evaluation Center of the University of Michigan, Ann Arbor, of the data transmitted to it from all the areas participating in the 1954 field trial of the Salk poliomyelitis vaccine in the U.S.A. Two distinct plans were used in the evaluation programme. (1) In the " observed study areas " all children in the second grade at school were vaccinated whose parents requested it (221,998), while the control subjects consisted of the children in the first and third grades who would have been vaccinated in similar circumstances (321,315) and those who would not (403,758). (2) In the " placebo areas " half the children in the 3 grades whose parents requested participation were vaccinated (200,745) and the other half, who acted as controls, were given a placebo (201,229). Children whose parents did not request participation were observed but were not used as controls, as a survey of the socio-economic status and reaction to health problems among families in the placebo areas indicated that the non-participating population differed from the participating and might well have a difference in resistance to poliomyelitis; this was borne out in the results. The total number of children studied was 1,829,916.

During the study period (from 2 weeks after the third injection to the end of the year) 428 cases of poliomyelitis or suspected poliomyelitis were reported in the placebo areas and 585 in the observed areas. According to defined criteria, 67·6% of these cases were classified as paralytic and 17·6% as non-paralytic poliomyelitis, and 14·8% as not poliomyelitis at all or doubtful. The incidence in the placebo areas of cases accepted as poliomyelitis was 28 per 100,000 among the vaccinated children and 71 per 100,000 among the controls. No difference was observed in the incidence of non-paralytic cases between the vaccinated and control children, but there were 3½ times as many paralytic cases among the controls as among the vaccinated children. In the observed areas there was no significant difference in the incidence of non-paralytic cases or doubtful cases between the vaccinated and control groups, but the incidence of paralytic cases was 17 per 100,000 among the former and 46 per 100,000 among the latter. The incidence of paralytic cases among the controls was less in the observed areas than in the placebo areas, but this difference disappeared if all the uninoculated children in the latter were included as controls.

No evidence was obtained to support the suggestion that an exaggerated incidence or localization of paralysis was associated with inoculation, there being no distinctive difference in the incidence in relation to time of cases between the various groups. Nor was there any indication of transmission of poliomyelitis virus from vaccinated persons to other members of the household during the 9 weeks after the date of the first inoculation.

In the placebo areas, there was a distinct tendency for the ratio between vaccinated and control subjects to increase with increasing severity of the paralytic involvement, and the difference in incidence of bulbospinal poliomyelitis between the two groups was pronounced and highly significant.

It was estimated that the vaccine had an effectiveness of 68% against infection with Type-1 poliomyelitis virus and of 90% or more against infection with Types 2 and 3. In the observed areas, the trend was the same but the figures slightly lower. *A. Ackroyd*

806. **Longevity in Abkhazia.** (Долголетние люди Абхазии)

I. B. SHAFIRO and S. D. GOGOKHIYA. *Советская Медицина* [*Sovetsk. Med.*] 51–56, No. 8, Aug., 1955.

The inhabitants of Abkhazia in Transcaucasia have long been noted for longevity, and this has recently been the subject of a special study by the Ministry of Health of the Abkhazian S.S.R. There are 2,144 persons over 90 years of age in this province, of whom 270 are over 100 and 11 over 120. This remarkable body of nonagenarians and centenarians includes members of many races—Abkhazians, Georgians, Russians, Ukrainians, Armenians, Poles, Greeks, and Turks—and of both sexes. Nearly all are agriculturalists and most live on the plain bordering the east coast of the Black Sea, a few live in the mountain villages and fewer still in the towns. Few of them are unmarried; most of them have enjoyed family life for 70 or 80 years, and as they are very virile and philoprogenitive they have large numbers of descendants—up to 150 in some cases. Thus there is little occasion for them to lack accommodation or care; they enjoy a good standard of living and maintain a high level of personal hygiene. They have a good and varied diet with plenty of milk, meat, vegetables, and fruit. Hardly any of them smoke, and they are very temperate, drinking no vodka and only moderate amounts of wine. They are industrious, active, and happy people, and many of them still work in their houses and fields, or on communal farms with the rest of their family.

As examples are cited Tulumdyan Varsenik Karakosovna, an old lady of 114 who lives in a 3-roomed house and helps in the housework and garden, as well as minding the toddlers (she has 3 sons and daughters—the eldest is 82—45 grandchildren, and about the same number of great-grandchildren, but cannot remember the exact number). Khatba Kharun Musovich, aged 124, has been a shepherd all his life and still accompanies the flocks to the mountain pastures. In 1948 a choir of men all aged over 100 took part in regional competitions. *L. Firman-Edwards*

Industrial Medicine

807. **The Identification of Accident Proneness**
K. T. JOHNSTONE. *Industrial Medicine and Surgery* [*Industr. Med. Surg.*] **24**, 293–295, July, 1955.

The author describes the apparent effects on accident incidence of interviewing each of 65 foundry workers who had reported accidents. Interviews lasted about 15 minutes and sought to determine how the accident had occurred. These men had sustained a total of 621 accidents between them in the preceding 2 months. In the next 2 months they had only 295 accidents, and the author claims that 54 (83%) of them showed immediate benefit from the interview procedure. Six illustrative case histories are given [from which it is evident that a good many of the accidents were directly due to faulty machinery, defective protective clothing, or ill-fitting goggles—factors that could easily be eliminated, with consequent reduction in the number of accidents]. The interviews also served to reveal workers who were poorly trained or lacked co-ordination at their work, and in one case indications of psychological maladjustment were found. In these instances immediate improvement was not to be expected, but identification enabled personal studies to be made.

As a means of detecting subjects for interview a measure of "expectable injuries" in a 2-month period was calculated on the basis of the average number of injuries for 2 months for the whole plant plus twice the square root of the average number of injuries. In this instance this calculation gave a figure of 3·66, so that any worker whose records showed 4 injuries or more in any 2-month period was regarded as accident-prone and in need of interview. *E. G. Chambers*

808. **Psychological Testing—Effect on the Accident Frequency of Bus Operators**
H. BRANDALEONE and E. FLAMM. *Industrial Medicine and Surgery* [*Industr. Med. Surg.*] **24**, 296–298, July, 1955. 1 fig., 11 refs.

In an effort to reduce the accident rate 178 new bus drivers engaged by a large operating company in New York were given the American Transit Association "motorability" examination and also a group of psycho-physical tests, mainly of a visual nature. In addition they were subjected to three psychological tests —the Thurstone Temperament Schedule, the Maslow Security–Insecurity Test, and the Standard Examination for Transit Employees, devised by Cleeton.

The 178 new drivers were divisible into 5 groups as follows: (1) 3 drivers took no tests; (2) 24 failed motorability tests and were not given psychological tests; (3) 51 passed motorability tests and were not given psychological tests; (4) 31 passed psychological tests and were not given motorability tests; and (5) 69 passed both motorability and psychological tests. Mean accident rates per man per month (A/M/M) over a period [not stated] were calculated for these groups, and showed a decrease from 0·609 A/M/M for Group 1 to 0·308 A/M/M for Group 5. Taking only "preventable" accidents—those regarded as being completely under the operator's control—the means ranged from 0·305 A/M/M for Group 1 to 0·117 A/M/M for Group 5. No relation was found between accident frequency and length of driving experience. Taking Group 3 as a control for Group 5 the authors compared the group accident rates of these two groups [presumably using the *t* test of significance] and found the difference to be significant at the 5% level. They conclude that the inclusion of psychological tests in the examination of applicants for jobs as drivers would result in the selection of men with a lower accident rate than did the previous method. They do not, however, claim that the tests used in this study are necessarily the most suitable or the most efficient. *E. G. Chambers*

809. **Long Term Observation of Chronic Benzene Poisoning.** [In English]
K. REJSEK and M. REJSKOVÁ. *Acta medica Scandinavica* [*Acta med. scand.*] **152**, 71–78, July 29, 1955. 26 refs.

Working at the Department of Industrial Medicine, Prague, the authors have examined periodically since 1931 a total of 4,538 persons exposed to benzene in their occupation. Since 1943, the examinations have included, in all cases, determination of the atmospheric concentration of benzene at the place of work and concentration of benzene in the subjects' urine and blood, as well as studies of the peripheral blood and bone marrow. The reactivity of the bone marrow was tested by observing the leucopoietic and leucocytic response to the injection of "pyrifer" vaccine, a preparation containing killed non-pathogenic strains of *Escherichia coli*.

Of the 4,538 persons examined, only 10 have exhibited severe haematological changes indicative of benzene poisoning; one of these died, but the remainder are well. The authors consider as serious pathological signs marked changes in the erythrocyte and leucocyte counts, particularly a neutrophil count below 2,500 per c.mm. and of long duration. In the one fatal case an early sign was a marked thrombocytopenia. Of the affected patients, 4 worked in the boot and shoe industry, 2 in rubber manufacture, and the others in the lacquer, aircraft, and pharmaceutical industries. The duration of exposure to benzene varied from 2 to 44 years and follow-up examinations were carried out periodically for 2 to 12 years after exposure to the hazard had been terminated by changing occupation.

Of the 9 surviving patients, all are without serious pathological changes and complain only of persistent and easily induced fatigue; in 3 cases there is increased capillary fragility, in 8 haematological deviations in the form of a neutropenia, while one patient is considered to have lessened resistance to infection. One patient is completely cured. *R. G. Meyer*

Radiology

RADIOTHERAPY

810. The Treatment and Prevention of the Leucopenia Caused by Radiotherapy with a New Thymonucleic Acid Extracted from Fish Roe—Deoxyribose Tetranucleotide. (Traitement et prévention des leucopénies roentgenthérapiques par un nouvel acide thymonucléique extrait de la laitance de poisson, le tétranucléotide à désoxyribose)
R. COLIEZ, A. N. LOISEAU, and R. SARFATI. *Presse médicale* [*Presse méd.*] **63**, 1137–1139, Aug. 27, 1955.

Deoxyribose tetranucleotide has been shown experimentally to be efficacious in the treatment of leucopenia resulting from irradiation. This substance is extracted from fish roe, the dried extract being made up into tablets each containing 0·05 g. of the active principle, and the dosage being 4 to 8 tablets daily.

Out of 389 cases of malignant disease (excluding leukaemia, Hodgkin's disease, and carcinoma of the thyroid gland) treated at the Hôpital Necker, Paris, with 200-kV *x* rays, leucopenia developed in 50. These 50 cases were divided into two groups. In the first group (29 cases) irradiation was stopped and deoxyribose tetranucleotide was given when the leucocyte count fell to 2,000 per c.mm. After 6 to 8 days the count began to improve and administration of the drug was stopped, irradiation being reinstituted when it reached 3,000 per c.mm.; the procedure was repeated if the count fell again. In the second group (21 cases) deoxyribose tetranucleotide was given in the same dosage when the leucocyte count fell to 3,000 per c.mm., but irradiation was continued, the drug being given for the remainder of the period of radiotherapy. In this group the leucopenia improved and the count remained at a satisfactory level throughout the remainder of the treatment period. *R. S. Pointon*

811. Glioblastomata Treated with Cobalt. (Glioblastomes traités par le cobalt)
A. JENTZER. *Neuro-chirurgie* [*Neuro-chirurgie*] **1**, 153–157, 1955. 4 figs., 1 ref.

The author describes a case of glioblastoma which was treated by the insertion on two occasions within 5 months of a radioactive cobalt source into the centre of the tumour. The total dose at 3 cm. from this point was calculated to be 21,500 r over the 5 months. It is claimed that radioactive cobalt has a selective action, in that the pyramidal cells and the normal astrocytes remain undamaged; this is thought to be due to the very hard gamma rays of cobalt, which are not stopped by nervous tissue to the same extent as the softer *x* rays. A further advantage of the method is that the healthy cerebral hemisphere receives very much less radiation from the cobalt than it does when two opposing *x*-ray fields are used, although the tumour dose from the radioactive cobalt was seven times that from conventional *x* rays. *Jan G. de Winter*

812. Moving-field Therapy of Carcinoma of the Oesophagus. (Bewegungsbestrahlung des Ösophaguskarzinoms)
F. WACHTLER. *Krebsarzt* [*Krebsarzt*] **10**, 193–199, Aug., 1955. 4 figs., 9 refs.

In carcinoma of the oesophagus treated by irradiation or by surgery a 5-year cure is rare—about 1% for either method—but palliation is usually possible and by the use of radiotherapy life may be prolonged for about 6 months. Intracavitary radium treatment is often impossible owing to stenosis, gives an unfavourable dose distribution, and carries the risk of ulceration and perforation. Deep *x* rays in tumour doses of 4,000 to 6,000 r give satisfactory palliation in about half the cases. The usual treatment with fixed fields gives a relatively poor tumour dose and a more severe general reaction; moving-field therapy is better, giving a more homogeneous tumour dose with a steeper fall-off to normal tissue.

Since 1953 this technique has been in use at the University Roentgen Institute in Vienna. Careful positioning of the patient is important, barium being used to locate the lesion and to ensure that it lies in the axis of rotation, so that the field may safely be narrow. Daily tumour doses of 150 to 200 r are given at 200 kV to a total of 5,500 to 7,000 r in 5 to 6 weeks. The skin dose is about one-third of this. A total of 30 patients have been treated, all with carcinoma of the oesophagus unsuitable for surgery. Passage of food was improved in 25 cases, and 10 patients have survived 6 to 16 months. In 28 cases the tumour dose was more than 4,000 r, an improvement over that attained with the fixed-field method. Some degree of palliation can be achieved with 3,000 r, but it is better to continue, even at some risk of perforation into a bronchus or of cardiac or pulmonary damage and late radiation pneumonitis. Still better results may be obtainable with supervoltage rotation therapy, but this remains to be seen. *J. Walter*

813. Effect of 2 Million Volt Roentgen Therapy on Various Malignant Lesions of the Upper Abdomen
R. J. GUTTMANN. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **74**, 204–212, Aug., 1955. 8 figs.

A brief report is presented from the Francis Delafield Hospital, New York City, of the results of irradiation in 40 cases of advanced malignant lesions involving the upper abdomen. The 2-million-volt *x*-ray unit was used with a filtration of 4 mm. of lead, equivalent to a half-value layer of 6·8 mm. of lead, and at a focus–skin distance of 100 cm. Two opposing fields were employed, the average field size being 15 × 15 cm. (range 10 × 10 cm. to 15 × 20 cm.). The tumour dose was from 4,000 r to 4,500 r in 4 to 4½ weeks, the skin dose ranging from 4,655 r to 5,215 r. In addition to 19 cases of primary

or metastatic carcinoma of the liver the series included 6 cases of carcinoma of the stomach, one case each of carcinoma of the duodenum and of the kidney, and cases of lymph-node and retroperitoneal sarcomata. In all cases the diagnosis was confirmed at biopsy.

Local reaction to treatment was limited to slight erythema and tanning. General tolerance was good, though assessment, particularly in relation to nausea and vomiting, was difficult since the patients were very ill. Diarrhoea was not observed and changes in blood count were not significant. Of the 40 patients, 9 died either during or shortly after completion of radiation therapy; of the remainder, 25 improved sufficiently to resume normal life for up to 2 years, while 6 obtained symptomatic relief.

A number of impressive case histories serve to show the value of this treatment in restoring comfort to the patient.

G. E. Flatman

814. **Malignant Disease of the Ovary and Radiotherapy. A Survey of 168 Cases with 10-Year Follow-up**

F. Ellis. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.* (*Lond.*)] 7, 1–10, July, 1955. 3 figs., 11 refs.

In a comprehensive paper the author analyses from many angles the treatment of ovarian carcinoma by radiotherapy and its results in 168 cases referred to the Sheffield National Centre for Radiotherapy from 1930 to 1943, and followed up for at least 10 years. The highest incidence of the disease was in the 4th and 5th decades. Cases were classified according to the histology and extent of spread of the disease.

The longest survivals were obtained where only the ovaries were affected without spread to other structures. It also appeared that ascites was of ominous prognostic significance in all cases except those in which only one ovary was involved. Pseudomucinous carcinoma carried the best prognosis, but the author draws attention to the value of Koltmeier's distinction between growths which show stromal invasion and those which do not, when histological classification seems to lose its significance. Pain and abdominal swelling are the most common presenting symptoms, and both may indicate a poor prognosis if not investigated early.

As regards surgical treatment, it is considered generally advisable to leave the uterus as a vehicle for intracavitary radium therapy unless this prejudices the surgical technique. A complete operation is held to carry a much better prognosis than an incomplete one, but "spill" at operation does not seem to have worsened the results in this series.

It is recommended that radiotherapy should be begun as soon as possible after operation. As regards technique, it seems that the best results are obtained when complete treatment is given with *x* rays and intrauterine radium, and that the results are poor when the uterus is left but not used for intracavitary radium therapy. Whether *x*-ray treatment should be confined to the pelvis and para-aortic lymph nodes or include the whole abdomen will depend on the extent of the disease and its histology. In addition, radioactive colloidal gold can be used where the peritoneal dissemination is considered to be microscopic, but this treatment should not be combined with abdominal baths.

Preoperative radiotherapy is recommended where the diagnosis is certain. Abdominal metastasis was found to be present in 116 out of 131 cases at the time of death.

R. D. S. Rhys-Lewis

815. **Survey of Cases of Carcinoma of the Ovary Treated in the Radiotherapy Department, London Hospital, 1943–1950**

W. Shanks. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.* (*Lond.*)] 7, 11–17, July, 1955. 3 figs.

In this paper are reviewed 170 cases of cancer of the ovary referred to the Radiotherapy Department at the London Hospital between April, 1943, and December, 1950. The maximum incidence of the disease occurred between the ages of 40 and 60. Though histological proof was not obtained in all cases, the subsequent course of the illness left little doubt of its nature. No attempt is made to classify the cases according to the customary histological groupings, the varied designations used in the case notes being retained. The symptomatology is equally varied, but pain, abdominal swelling, and discomfort were predominant.

Surgical removal, when possible, is considered the method of choice, and this is followed by postoperative radiotherapy. The best prognosis was obtained where both surgery and radiotherapy were complete, 10 of 18 patients (55%) so treated surviving 3 years. Where complete local removal was combined with panhysterectomy and complete radiotherapy the 3-year survival rate was 53% (17 out of 32). The author points out that this suggests that there is little advantage to be gained by removal of the uterus. Incomplete surgery followed by radiotherapy gave a 3-year survival rate of 42·5% (14 out of 32), and when both radium and *x* rays were used the rate was 50% [no figures given]. There were no 3-year survivals where apparently complete surgery was followed by incomplete radiotherapy, and no patient survived one year when both surgery and radiotherapy were incomplete. Undifferentiated tumours also carried a very bad prognosis.

The technique of postoperative radiotherapy was wide-field irradiation of the whole abdomen with 3 fields to a dose of 3,000 r in 5 weeks under haematological control. A few cases also had treatment with radium, 2 standard Stockholm doses being given. The main cause of death was carcinoma of the peritoneum.

The author concludes by describing a method and apparatus for administering intraperitoneal colloidal gold in terminal cases of ascites.

R. D. S. Rhys-Lewis

816. **Experiences in the Use of Radio-active Colloidal Gold in the Treatment of Carcinoma of the Ovary**

C. L. Lewis. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.* (*Lond.*)] 7, 17–19, July, 1955. 1 ref.

The author describes the use of radioactive colloidal gold (^{198}Au) in the treatment of malignant disease of the ovary at the United Oxford Hospitals. ^{198}Au has a half-life of 2·7 days, and emits both beta rays with an

energy of 0·96 MeV and gamma rays of 0·411 MeV. Intraperitoneal instillation of ^{198}Au would seem an ideal method of treating peritoneal deposits from carcinoma of the ovary, but unfortunately the beta emission far outweighs the gamma radiation, and as the beta particles have a range of only 3·8 mm. in water, this severely limits the size of any deposit which could be adequately irradiated. Secondly it is difficult to be sure that the ^{198}Au is uniformly distributed over the peritoneum in adequate concentration.

An attempt has been made to overcome the first of these difficulties by selection of cases, and the second by working out a careful technique of administration. This is described in detail. A standard intraperitoneal saline drip apparatus is set up, but fitted with a cannula instead of a needle, and after a preliminary paracentesis 125 to 150 mc. of ^{198}Au is instilled into the drip while 200 to 300 ml. of saline is being injected. Strict radioactive precautions are observed during the instillation, which takes about a minute. The patient is then placed in various positions as suggested by Walton and Sinclair (*Brit. med. Bull.*, 1951, **8**, 165) and survey counts are made.

Although the method has not yet been used extensively, the author concludes that it has a definite if limited place both in the radical and in the palliative treatment of microscopic invasion of the peritoneum by carcinoma of the ovary. *R. D. S. Rhys-Lewis*

817. **Treatment of Multiple Myeloma with Radioactive Iodine and Radioactive Iodinated Serum Albumin**
J. P. Kriss, H. R. Bierman, S. F. Thomas, and R. R. Newell. *Radiology* [*Radiology*] **65**, 241–249, Aug., 1955. 4 figs., 10 refs.

The systemic treatment of cases of multiple myeloma with radioactive iodine (^{131}I) and radioactive iodinated serum albumin (R.I.S.A.) is here described from Stanford University School of Medicine, San Francisco.

One group of 9 patients aged 40 to 70 years received a total of 24 treatments with ^{131}I, about 150 mc. of the isotope being given at each treatment. Loss of circulating ^{131}I to the thyroid gland was prevented by administration of a dose of stable potassium iodide daily for 5 days before and 7 days after treatment. In 4 patients in this group there was relief of pain with gain in weight. Another group of 7 patients were treated by intravenous injection of 10 to 20 mc. of R.I.S.A., the number of injections in this group being 12. Saturated potassium iodide solution, 5 drops daily, was given for 3 weeks after treatment to protect the thyroid gland from the ^{131}I which is slowly released from the albumin. In 3 cases there was marked relief of pain.

Discussing the over-all results, the authors state that relapse generally occurred in 3 to 4 months but that re-treatment was usually effective. Anaemia did not improve, no permanent change was observed in the serum protein pattern, and there was no recalcification of bony lesions. Radiation sickness occurred in one-third of the cases. It is suggested that treatment with ^{131}I or R.I.S.A. should be given: (*a*) when whole-body irradiation is desired; (*b*) if the patient cannot be moved easily for *x*-ray therapy; (*c*) if local *x*-ray therapy is inadvisable because painful areas are too numerous; and (*d*) if skin tolerance to *x* rays has been exhausted.

Clinical details are given in a table, and the paper includes illustrations of scanned whole-body contours. Graphs showing the blood levels of ^{131}I and R.I.S.A. are reproduced. It is emphasized that in patients with renal insufficiency body retention and the blood level of ^{131}I remain high; such patients, therefore, may be seriously overdosed if given 150 mc. of the isotope, though such a dose can be tolerated by patients with normal renal function. It is pointed out that treatment in these cases is merely palliative and life is not prolonged thereby. *G. E. Flatman*

RADIODIAGNOSIS

818. **Diagnosis of Infrapulmonary Pleural Effusion**
J. W. Wilson. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 1423–1427, Aug. 20, 1955. 6 figs., 16 refs.

The purpose of this paper is to draw attention to the infrapulmonary type of effusion in the pleural cavity, which, as the author points out, is " neither rare nor uncommon ", he having collected 24 cases from the files of the department of radiology at Parkland Hospital, Dallas, Texas, over a period of 8 months.

When fluid has collected in the pleural space beneath the lung and above the diaphragm the appearances in the postero-anterior radiograph taken in the erect position suggest elevation of one or other dome of the diaphragm. On screening in the expiratory phase the fluid is pushed up from beneath the lung and assumes the ordinary classic appearance of a pleural effusion; but the easiest way to reach a diagnosis, according to the author, is to have films taken in the decubitus or supine position, when the fluid will be seen to have gravitated to a different situation. As a rule the amount of effusion is not very large, though in one of the cases reported some 700 ml. was aspirated. The accumulation of fluid in this situation does not appear to depend on the type of fluid; thus this may consist of exudates or transudates, of serous or purulent effusions, or even of blood. The author points out that, although the amount of effusion may be comparatively small, as it collects at the base there may be considerable interference with respiratory function.

Recommendations as to treatment are given.
L. G. Blair

819. **Reduced Intrathoracic Circulation as an Aid in Angiocardiography. An Experimental Study**
I. Boerema and J. R. Blickman. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **30**, 129–142, Aug., 1955. 10 figs., 21 refs.

Many of the difficulties still encountered in angiocardiography are considered to be due to rapid dispersal of the contrast medium and the great mobility of the walls of the heart and great vessels during the cardiac cycle. This has necessitated the rapid injection of a

concentrated medium and the use of expensive apparatus to obtain serial radiographs by frequent, short exposures. These difficulties could be overcome if the blood flow through the heart were reduced during the examination.

The effect of respiration on the circulation has been discussed by a number of authorities since Valsalva's original observation, notably by Weber who, in 1850, showed that forced expiration when the glottis was closed was followed by immediate cessation of the heart beat with rapid weakening and disappearance of the radial pulse; he concluded that this was due to compression of the venae cavae and right atrium. This observation has since been confirmed, and the present authors, at the University of Amsterdam, carried out experiments on animals to determine whether the mechanism described by Weber could safely be utilized in angiography in the human subject. The trachea was intubated with a cuffed tube and a water manometer was placed in the anaesthetic circuit so that exact control of the pressure exerted by manual compression of the bag was possible. A pressure of 30 to 60 cm. of water produced the desired decrease in cardiac output. Direct blood-pressure recordings were obtained from different positions under varying conditions. The technique and results of the experiments are described and angiocardiograms are reproduced.

[This is an interesting and thoughtful study which may be of considerable value.] *Sydney J. Hinds*

820. **The Roentgen Appearance of the Pulmonary Veins in Heart Disease**

H. L. Steinbach, T. E. Keats, and G. E. Sheline. *Radiology* [*Radiology*] **65**, 157–168, Aug., 1955. 10 figs., 7 refs.

In the postero-anterior radiograph of the chest the veins of the right lower lobe and, less frequently, those of the right upper lobe and left lower lobe can be distinguished. The lateral view shows the superimposed shadows of both lower-lobe veins converging towards the posterior aspect of the left auricle. In the left anterior oblique view the main venous trunks of the right lung are superimposed on the heart below and slightly posterior to the pulmonary artery. The smaller venous branches from the lung converge towards the main trunks like the spokes of a wheel. Similarly in the right anterior oblique view the veins of the left lung may be identified through the heart shadow.

It is of great importance to assess the degree of vascularization of the lungs in the diagnosis of heart disease, and this may in some cases cause considerable difficulty. The authors, at the University of California School of Medicine, San Francisco, therefore made an attempt to evaluate separately the pulmonary arteries and veins. In pulmonary stenosis they have found that, although the main pulmonary artery is dilated and the hilar branches may appear normal, the pulmonary veins are smaller than normal. In one instance in which a clinical diagnosis of pulmonary stenosis was made large pulmonary veins were found, and catheterization showed that the stenosis was complicated by a patent ductus and by an anomalous pulmonary vein entering the right auricle. The demonstration of small pulmonary veins has also been helpful in cases of Fallot's tetralogy, tricuspid atresia, and truncus arteriosus. Enlargement of the veins was found in many instances of left-to-right shunt. In a survey of 100 proved cases of patent ductus arteriosus visible enlargement of the pulmonary veins was observed in 71.

In acquired mitral valve disease with pulmonary hypertension the pulmonary veins in general appear normal. This, it is considered, is due to the narrowing of the peripheral pulmonary arteries which has been shown to occur in pulmonary hypertension secondary to mitral stenosis. *Kenneth A. Rowley*

821. **Transhepatic Venous Catheterization and Venography**

H. R. Bierman, K. H. Kelly, L. P. White, A. Coblentz, and A. Fisher. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 1331–1334, Aug. 13, 1955. 5 figs., 6 refs.

The largest and most accessible branches of the portal vein lie within a narrow arc from the linea alba at the level of T12. Transhepatic portal venepuncture was attempted 144 times in 73 patients, portal venous blood being obtained in all except 9; in one case of neurofibromatosis 5 separate attempts failed. Venograms were obtained after " forcible injection " of 20 to 50 ml. of 70% contrast medium, sodium acetrizoate, diodone, or sodium iodomethamate being found satisfactory for this purpose. In 14 cases a polyethylene catheter was introduced through the needle and allowed to remain for 2 to 19 days; there were no sequelae, although portal blood clotted readily so that heparin sodium had to be used. Many of the patients had widespread neoplastic disease and follow-up until death was possible in 62 of the 64 cases, necropsy being performed in 55. [No further mention is made of the 9 patients in whom venepuncture failed.] There were no serious complications. Arterial blood was aspirated in 2 cases and intestinal contents in 3; in one case the gall-bladder was visualized by direct puncture and in another the cystic duct was entered and catheterized. In 3 cases a haematoma was found at necropsy, but in only one of these were there serious symptoms. While the normal intraportal pressure rarely exceeds 10 cm. H_2O, pressures up to 22 cm. were observed in patients with portal cirrhosis or intrahepatic portal obstruction, and during Valsalva's manœuvre or the act of vomiting. The venograms showed that in the liver containing metastases the large portal branches are sharply diverted around large areas which are supplied mainly by the hepatic artery. The authors state that there is " relatively less venous circulation in and immediately about the metastatic area " and that the superimposition of vascular patterns at different levels throughout the liver tends to obscure many areas of small metastases. *Denys Jennings*

See also Gastroenterology, Abstract 660; Neurology and Neurosurgery, Abstract 773.